DOWNBEAT NYSTAGMUS: CHARACTERISTICS AND LOCALIZATION OF LESIONS*

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INTRODUCTION

PATHOLOGIC NYSTAGMUS CONSISTS OF INVOLUNTARY, RHYTHMIC OSCILLATIONS of the eyes in which smooth movements carry the eyes away from their intended positions of gaze. In jerk nystagmus the slow component (smooth movement) takes the eyes away from the target. The fast component (saccade) brings the eyes back toward the target. The direction of the fast component establishes the direction of the nystagmus. Although there are many types of nystagmus, specific types can be identified by careful observation of such characteristics as waveform, direction, effects of gaze position, effects of fixation, and conjugacy.[1-4] Identification of nystagmus can be useful in localizing lesions in the central nervous system (CNS). The association of nystagmus and location has usually been made by correlating the nystagmus with findings from clinical and pathologic examinations. In some instances experimental lesions in animals have confirmed the association.

Most pathologic types of nystagmus are in the horizontal direction. Vertical nystagmus received relatively little attention in the early medical literature. For example, Boehm[5] did not discuss vertical nystagmus in his treatise on nystagmus in 1857. Most early medical writers considered vertical nystagmus to be rare. In 1908 Fuchs[6] wrote, "True nystagmus is nearly always bilateral and then the movements are almost invariably equal, simultaneous, and parallel in the two eyes. Bilateral nystagmus is usually horizontal, less often rotary or mixed. Vertical bilateral nystagmus is rare." Wilbrand and Saenger[7] reviewed nystagmus extensively in their textbook in 1921. They noted that vertical nystagmus can be produced in experimental animals by sectioning the anterior vertical semicircular canal in the labyrinth. Vertical nystagmus was described briefly in some patients with severe bilateral loss of vision, drug toxicity (barbiturates and quinine), multiple sclerosis, spasmus nutans, lesions of the pons and

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medulla (tuberculoma and meningioma), and encephalitis lethargica. However, the characteristics of the nystagmus were usually not described.

Berens and McAlpine[8] stated in 1950, "Bilateral vertical or mixed movements of nystagmus are rare. . . . Unfortunately the direction of the nystagmus has no diagnostic value, and the most important clinical problem is the differential diagnosis as to whether it is peripheral or central." Other authors believed that the direction of nystagmus was significant and could be used to distinguish vestibular nystagmus caused by lesions of the peripheral vestibular system from that caused by lesions in the brainstem. They believed that purely vertical nystagmus was almost always due to lesions in the brainstem.[9,10] A lesion is not likely to affect only the vertical semicircular canals or their afferent axons in the vestibular nerves. Lesions of the labyrinths and the vestibular nerves produce nystagmus with horizontal, vertical, and torsional components. Walsh[11] reviewed what he considered to be the clinically important aspects of nystagmus in his textbook in 1947. He described observations by another author of 200 patients with nystagmus. The direction was horizontal in almost 50%, rotatory in 15%, vertical in 12%, mixed in 4%, torsional in 2%, and convergent, divergent, disconjugate, or unclassified in 15%. He noted that vertical nystagmus can be unilateral in spasmus nutans and in uniocular loss of vision.

Walsh[11] described a characteristic form of "cerebellar" or "central" nystagmus that was associated with disorders of the cerebellum. He described a horizontal, gaze-evoked form where the nystagmus is not present in primiary gaze, but occurs in lateral gaze with the slow component toward primary gaze and the fast component toward the direction of gaze. He also described vertical nystagmus in two children with the Arnold-Chiari malformation, and thought the nystagmus was characteristic. He wrote, "A symptomatology of nystagmus, cerebellar ataxia, bilateral pyramidal tract involvement and hydrocephalus in a patient with normal eyegrounds should suggest the possibility of this defect." However, other characteristics of the nystagmus were not described.

O'Brien and Bender[12] in 1945 and Bender and Gorman[13] in 1949 were among the first authors to draw a distinction between vertical nystagmus in upgaze and vertical nystagmus in center gaze. They stated that vertical nystagmus in upgaze was not uncommon and was indicative of acquired lesions of the brainstem. In contrast, they believed that most cases of vertical nystagmus in center gaze were due to congenital nystagmus and that the cause was rarely an acquired lesion in the brainstem or cerebellum. They described upbeat nystagmus in center gaze and vertical oscillopsia in two chronic alcoholics. Authorities have disagreed about

whether or not lesions confined to the cerebellum can produce nystagmus.[14] Some believe that although nystagmus is frequently associated with cerebellar lesions, it is caused by damage to the nearby vestibular nuclei, vestibular nerves, or brainstem. Others believe that pure cerebellar nystagmus does exist.

In 1954 Cogan and Barrows[15] described the neuro-ophthalmic abnormalities in nine patients with platybasia or Arnold-Chiari malformation. They found vertical nystagmus in all patients. It was present in center gaze in eight. The direction of the fast component was described in only two patients. Both had downbeat nystagmus (DBN). In DBN the slow component is upward and the fast component (saccade) is downward. In one patient DBN was observed in center gaze and decreased during reading (convergence). In the other, DBN was not present in center gaze but was present in lateral gaze. All but one of the nine patients had symptoms and signs of cerebellar damage. Compression of the brainstem and/or cerebellum was thought to cause the ocular motor abnormalities. Malis and colleagues[16] had also described a high prevalence of nystagmus in patients with the Arnold-Chiari malformation.

In 1968, Cogan[17] published the first study to describe systematically the characteristics, causes, and localization of DBN. Almost all of the patients in his study (21 of 27) had nystagmus in center gaze. The effects of eccentric gaze on the nystagmus were variable. DBN was present in lateral gaze in 14 patients, and in 4 of these was greater in lateral gaze than in center gaze. DBN was observed in down gaze in 24 patients, and increased in this position compared to center gaze in 8. DBN was found in upgaze in only seven patients, but was greatest in this position in one patient. The nystagmus was affected by positioning of the head or body in most patients in whom this was tested. Horizontal optokinetic nystagmus (OKN) was absent or diminished in all but one of the patients in whom it was tested. This observation indicated that the smooth tracking eye movement system (smooth pursuit) was impaired. A variety of causes was found, including developmental anomalies of the cervical spine and base of the skull (platybasia and Arnold-Chiari malformation), multiple sclerosis, tumors, alcoholic cerebellar atrophy, and ischemia. The most common symptoms were oscillopsia or blurring of vision due to the nystagmus and difficulty in gait due to ataxia or impairment of the corticospinal tracts. The symptoms, the signs on neurological examination, and the findings in radiologic test and during surgery, led Cogan to suggest that lesions producing DBN might be localized to the cerebellum or lower brainstem.

In the past decade, accurate electronic methods of recording eye movements have been used to study eye movements in normal human subjects

and patients with abnormal eye movements.[18] Several studies have described analyses of recordings in patients with DBN.[19-22] The largest of these, by Halmagyi and colleagues,[23] presented the findings from clinical examinations and eye movement examinations in 62 patients with DBN. Electro-oculography (EOG) was used to record the nystagmus in 38 patients and to measure vertical pursuit in 17. Horizontal pursuit, OKN, and vestibulo-ocular responses (VOR) were not measured systematically. Their study confirmed Cogan's observations that a variety of disorders can cause DBN and that neurologic symptoms and signs usually indicated that cerebellar lesions were present. The most frequent disorders were Arnold-Chiari malformations, hereditary and sporadic cerebellar degenerations, and other acquired cerebellar degenerations (alcoholic, paraneoplastic, and anoxic). The characteristics of DBN were thoroughly described. The researchers concluded that an increase in slow-component velocity in lateral gaze is characteristic of DBN and documented that positioning of the head increased DBN in most of the patients tested (23 of 37 patients).

Studies in experimental animals have also supported localization of DBN to the cerebellum. Lesions of the posterior midline structures of the cerebellum have produced DBN and/or positional nystagmus. Spiegel and Scala[24,25] found that lesions of the cerebellum could produce vertical nystagmus in cats. Cauterization or extirpation of the posterior vermis caused spontaneous upbeat and DBN that could be modified by positioning of the head and body. Fernandez and colleagues[26-28] produced positional nystagmus in cats with lesions of the nodulus. Takemori and Suzuki[29] produced DBN and impaired horizontal OKN in rhesus monkeys with bilateral lesions of the flocculi. Zee and colleagues[30] removed the flocculi of rhesus monkeys and caused DBN that increased in lateral gaze. Histopathologic examination in these studies indicated that the experimental lesions were usually confined to the structures of the caudal cerebellum. However, deJong and co-workers[31] have shown that a section through the midline of the medulla can produce DBN in the monkey.

As quantitative recordings of eye movements have been used in increasing numbers of patients, several patterns of eye movement abnormalities have been identified that are characteristic of lesions at specific locations in the CNS or of specific disorders.[18] The pattern associated with cerebellar lesions consists of (1) fixation instabilities, such as upbeat nystagmus, DBN, rebound nystagmus, macro-square wave jerks, ocular flutter, and opsoclonus; (2) saccadic dysmetria; (3) impaired smooth pursuit; (4) defective OKN; (5) abnormally high VOR; and (6) impaired visual-vestibular interactions, such as inability to suppress VOR with fixation.[20,32-35] Impaired smooth pursuit and abnormal visual-vestibular interactions probably result from damage to the flocculi and/or vermis,

since experimental lesions of these structures in the monkey produce these abnormalities.[30,36-38] However, eye movement systems have not been systematically studied with electronic recordings in a large number of patients with DBN to assist in localizing lesions.

The objective of this thesis was to study the clinical examination and electronic recordings of eye movements of a large number of patients with DBN to (1) identify the etiologies, (2) describe the characteristics of DBN, and (3) establish the location of lesions causing DBN.

MATERIALS AND METHODS

PATIENTS AND NORMAL SUBJECTS

The computerized data files of the clinical eye movement laboratories at the UCLA Medical Center were searched for patients with DBN who had eye movement recordings from July 1976 through June 1986. DBN could be present in any direction of gaze and in any position of the body and head. The data files for the same 10-year period were also used to identify patients with isolated midline cerebellar atrophy who did not have DBN. Atrophy of the cerebellar vermis was demonstrated by computed tomography (CT) scanning or magnetic resonance imaging (MRI). No atrophy or other abnormalities of the brainstem were found by these neuroimaging studies. The results of the eye movement recordings in these patients were compared with those of the patients with DBN. A group of normal subjects, who had no neurologic disorders, was also studied. Informed consent was obtained after the nature and purpose of the study were explained.

CRITERIA FOR IDENTIFYING ETIOLOGY BY CLINICAL EXAMINATION

Almost all patients were referred to the laboratories by neurologists. Each patient's history, neurologic examination and laboratory tests, including neuroradiologic tests such as pneumoencephalography, CT scan, and MRI, were reviewed. In addition, all patients were examined by a neurologist on the research team. Data from the clinical examination, *excluding* eye movement recordings, were used to determine causes and locations of CNS lesions.

The following are examples of the criteria used to identify etiologies:

Infarction was suggested by a sudden onset of symptoms and signs in patients who had systemic vascular disorders, such as diabetes mellitus, hypertension, or arteriosclerosis. Arteriosclerosis was suspected if an elderly patient had previous evidence of coronary artery or peripheral vascular occlusive disease. It was also suspected if an elderly patient

without a history of previous occlusion had a clinical course typical of infarction and was thought not to have other predisposing conditions. The clinical course was characterized by stability with no improvement or a partial, gradual improvement. Cerebral angiography and noninvasive flow studies of the carotid arteries were obtained in some patients. Neuroimaging was used to identify infarcts in the CNS.

Cerebellar and spinocerebellar degeneration (idiopathic, sporadic, or hereditary) was indicated by a gradual onset and gradual progression of signs and symptoms. Other conditions that can cause a similar clinical course, such as tumor, multiple sclerosis, toxicity and encephalitis, were not present. CT scanning and MRI often demonstrated a small cerebellum, lower brainstem, and/or spinal cord. *Developmental anomalies*, such as Arnold-Chiari malformations—caused signs and symptoms at birth or in adulthood. Their onset was sudden or gradual, and the course was stable or gradually progressive. Neuroradiologic studies, such as CT scanning with or without intrathecal metrizamide, MRI, pneumoencephalography, and myelography, demonstrated the anomalies.

Multiple sclerosis (MS) was suggested by the sudden or subacute onset of focal CNS signs and symptoms in a young adult with an exacerbating-remitting course. Recurrences indicating lesions at other sites in the CNS were present. Laboratory tests, such as cerebral spinal fluid (CSF) examination, visually-evoked potentials (VEP), and brainstem-evoked responses, were obtained. CT scanning was performed to identify other causes, and MR scanning revealed lesions consistent with demyelinating plaques in the cerebral hemispheres, brainstem, or cerebellum in some patients. Patients were categorized with diagnostic criteria recommended by Poser and colleagues.[39] Patients identified as having MS had either clinically definite disease or probable disease as supported by laboratory findings.

CRITERIA FOR LOCALIZATION OF LESIONS

The localization of lesions was made by correlating signs and symptoms from the neurologic examinations performed by neurologists with accepted concepts of functional neuroanatomy. DBN and the results of eye movement recordings were *not* used for this localization. Truncal ataxia, gait ataxia, dysmetria of the limbs, dysrhythmia of rapid alternating limb movements, and scanning speech were considered to be characteristic of cerebellar lesions. Abnormal limb movements and gait due to paresis and sensory loss affecting the limbs and dysarthria were not considered to be characteristic of cerebellar damage.

Localization of lesions to the pons and cerebellum by clinical examination is often imprecise. For example, lesions in the pons can disrupt

afferent or efferent pathways of the cerebellum, causing the same signs and symptoms as noted above. However, these lesions will usually produce other deficits indicating damage to the pons. The localization for these lesions was classified in this study as cerebellum and pons, possibly causing an overestimation of the frequency of cerebellar lesions. All the etiologies identified in this study can cause damage at several locations simultaneously, for example, the cerebellum and the brainstem. It is often impossible to differentiate between lesions of the pons that affect afferent or efferent pathways to the cerebellum and separate lesions at both sites.

EYE MOVEMENT RECORDINGS

Horizontal movements of each eye were recorded with direct current (DC) EOG. Active Ag/AgCl electrodes were placed at the inner and outer canthi, and a reference electrode was located at the midline of the forehead. The bandwidth of this system was 0 to 42 Hz. In most patients vertical eye movements were also recorded with EOG. Electrodes were placed above and below the eyes. EOG and recording methods that use reflection of infra-red light from the surface of the eye can cause artifacts when recording vertical movements.[40] Therefore, a modified, magnetic search coil technique that can record vertical movements without these artifacts was used in some patients.[41] The bandwidth of this system was 0 to 1600 Hz. In the search coil technique, the patient was seated within 3-foot-diameter horizontal and vertical pairs of induction coils. A topical anesthetic was placed on the eye. An annulus of soft plastic contact lens material, in which the detection coil was embedded, was then placed on the sclera. Analog signals were displayed on a polygraph, stored on FM magnetic tape, and digitized at 200 samples/sec by an on-line computer. Programs were used to compute the position, amplitude, and velocity of the eye. The computer controlled the stimuli during tests of smooth pursuit, saccades, OKN, VOR to rotation, and visual-vestibular interactions. The computerized stimulation and recording systems have been described in detail previously.[42]

Parameters of DBN, such as mean frequency, mean amplitude, mean velocity, and waveform of the slow component, were measured in each patient. These observations were made in center gaze, horizontal gaze at 30° and vertical gaze of 30°. Fixation targets were placed at distances of 2 m and 25 cm. The effects on nystagmus parameters of loss of fixation (eyes opened in the dark in the sitting position), static positioning of the body and head in supine and lateral positions, and rapid positioning (Hallpike maneuvers) were measured. To test tracking, a helium-neon laser was mounted behind the patient and a 0.4° diameter red target was

reflected from a mirror mounted on a galvanometer onto a white screen in front of the patient. To induce horizontal saccades, the laser target moved in unpredictable square wave patterns. The amplitude, peak velocity, and latency of saccades were calculated. To induce pursuit, the target moved in sinusoidal patterns of 0.1 Hz and 11.3°/sec (peak velocity), 0.2 Hz and 22.6°/sec, and 0.4 Hz and 45.2°/sec. Horizontal pursuit was measured by EOG or search coil in all patients. The gain of smooth pursuit was calculated as peak eye velocity/peak target velocity.

OKN was produced by seating the patient within a 1-m-diameter drum. The interior of the drum was decorated with 3°-wide, white vertical stripes placed every 15° on a black background. The patient was instructed to focus on white stripes as they passed directly in front of him. The drum was rotated at constant velocities of 30°/sec and in sinusoidal patterns of 0.2 Hz and 22.6°/sec (peak velocity) and 0.05 Hz and 60°/sec. The OKN gain was calculated (peak slow component velocity/peak drum velocity). Horizontal VOR were produced by rotating the patient in a motorized chair in the dark. The patient was instructed to perform arithmetic calculations. The chair was rotated sinusoidally at 0.2 Hz and 22.6°/sec (peak velocity) and 0.05 Hz and 60°/sec. The VOR gain was calculated. Synergistic visual-vestibular interaction—the visual-VOR (VVOR)—was induced by rotating the patient within the lighted stationary OKN drum. Smooth pursuit and OKN slow components were in the same direction as the VOR slow components. Antagonistic visual-vestibular interaction—suppression of VOR by fixation (VORfix)—was produced by rotating the patient in the dark while asking the patient to fixate a small, red, light-emitting diode attached to the chair. During visual-vestibular interaction tests the chair was rotated at the same frequencies and velocities as in the VOR tests. The visual-vestibular interaction gains were calculated.

RESULTS

PATIENTS AND NORMAL SUBJECTS

Ninety-one patients with DBN were studied during the 10-year period. Their mean age was 50.2 years (standard deviation [SD], 17.6; range, 13 to 82). Demographic information, diagnoses, and localizations from the clinical examination for all of the DBN patients are presented in Table I. During the same period, 11 patients with cerebellar atrophy who did not have DBN were found. The mean age of this group was 51.3 years (SD, 17.8; range, 23 to 78). Nineteen normal subjects composed a control group for comparison of electronically recorded eye movements. Their

TABLE I: DIAGNOSES, LOCALIZATIONS BY CLINICAL EXAMINATION, AND OTHER EYE MOVEMENT ABNORMALITIES IN DBN PATIENTS

PATIENT	AGE-SEX	ETIOLOGY	LOCALIZATION	EYE MOVEMENTS
1	79 F	INF	CE + PO	1
2	73 F	INF	CE	—
3	63 F	INF	CE	1
4	64 M	INF	CE + PO	—
5	57 M	INF	CE + PO	—
6	48 F	INF	CE + PO	—
7	57 M	INF	CE	—
8	81 F	INF	CE + PO	—
9	60 M	INF	CE	1
10	74 F	INF	CE	—
11	71 M	INF	CE + PO	3
12	25 F	INF	CE + PO	1,2
13	51 F	INF	CE	—
14	52 F	INF	CE + PO	1,2,4
15	64 F	INF	CE	1,2
16	72 M	INF	CE	1
17	68 F	INF	CE	1
18	78 F	INF	MI	1,7
19	60 F	INF	PO	—
20	73 F	INF	CE	1
21	64 M	INF	CE + PO	1
22	41 F	INF	CE + PO	1
23	74 F	INF	CE	—
24	23 F	DEG	CE + PO	6
25	82 F	DEG	CE	1,2
26	35 F	DEG	CE + PO	1
27	59 F	DEG	CE + PO	1
28	74 M	DEG	CE + PO	1,5
29	34 M	DEG	CE + PO	1,2,4,6
30	61 M	DEG	CE + PO	1,2
31	47 M	DEG	CE	1,2
32	21 M	DEG	CE	—
33	19 F	DEG	PO	3
34	67 F	DEG	CE + PO	1,5
35	50 F	DEG	CE	1,2,4
36	43 F	DEG	CE + PO	1,2,4
37	62 M	DEG	CE + PO	1,2
38	63 M	DEG	CE	1,2,4
39	65 F	DEG	CE + PO	—
40	57 F	DEG	CE	1,5
41	62 M	DEG	CE	1
42	64 F	DEG	CE	1,2
43	49 M	DEG	CE	1,2
44	66 F	DEG	CE	1
45	68 M	DEG	CE	1,2
46	27 F	MS	CE + PO	1,3,8
47	24 F	MS	CE	—
48	35 F	MS	PO	1,3
49	37 F	MS	CE	1,2
50	48 F	MS	CE + PO	1,2,3,6
51	65 F	MS	CE	5

TABLE I: DIAGNOSES, LOCALIZATIONS BY CLINICAL EXAMINATION, AND OTHER EYE MOVEMENT ABNORMALITIES IN DBN PATIENTS (CONT'D)

PATIENT	AGE-SEX	ETIOLOGY	LOCALIZATION	EYE MOVEMENTS
52	34 F	MS	CE + PO	1,4
53	41 M	MS	CE + PO	3
54	46 F	MS	CE + PO	—
55	60 F	MS	CE + PO	1,2,4
56	60 F	MS	CE	1,2
57	50 M	MS	CE	1,2
58	22 F	MAL	CE	1,2,4
59	48 F	MAL	PO + ME + SP	1
60	43 F	MAL	CE	—
61	36 F	MAL	CE	—
62	25 M	MAL	CE	1,2
63	50 F	MAL	CE	1,2
64	41 M	MAL	ME + SP	1
65	13 M	MAL	CE	1,2
66	15 M	MAL	CE	1,2
67	26 M	MAL	CE + PO	—
68	29 F	MAL	CE	1,2
69	64 F	TOX	TE	1
70	42 F	TOX	TE	1
71	77 F	TOX	TE	1,2
72	72 F	TOX	TE + CE	—
73	50 M	TRA	CE + PO	3
74	25 F	TRA	CE + MI	7
75	29 F	TRA	CE	1,2
76	50 F	NEO	CE + PO	1,2,5
77	55 F	NEO	CE	—
78	26 M	NEO	CE + MI	7
79	54 M	ALC	CE	1
80	35 F	ALC	CE + PO	1
81	45 F	AVM	CE	1
82	54 F	AVM	CE + PO	6
83	48 M	AIDS	CE	1,2
84	20 M	FAM	CE	—
85	31 M	ENC	MI	7,8
86	55 M	RAD	CE + PO	6
87	55 M	?	CE	—
88	66 M	?	CE	1,2,4
89	29 M	?	CE	1
90	50 M	?	CE	1,2
91	38 F	?	CE	1

INF = infarction, DEG = degeneration, MS = multiple sclerosis, MAL = malformation, TOX = drug toxicity, TRA = trauma, NEO = neoplasm, ALC = alcoholism, AVM = arteriovenous malformation, FAM = familial ataxia syndrome, RAD = radiation, ? = not known.

CE = cerebellum, PO = pons, MI = midbrain, ME = medulla, SP = spinal cord, TE = temporal lobe.

1 = horizontal, gaze-evoked nystagmus, 2 = horizontal, rebound nystagmus, 3 = internuclear ophthalmoplegia, 4 = horizontal, saccadic hypermetria, 5 = horizontal, saccadic hypometria, 6 = horizontal gaze palsy, 7 = vertical gaze palsy, 8 = peripheral, 6th cranial nerve palsy.

TABLE II: DIAGNOSIS FROM CLINICAL EXAMINATION IN DBN PATIENTS

DIAGNOSIS	FREQUENCY (%)	NO.
Infarction	25	23
Cerebellar degeneration, spinocerebellar degeneration	24	22
Multiple sclerosis	13	12
Developmental anomaly (Chiari, basilar invagination, syringobulbia)	12	11
Drug toxicity (phenytoin, carbamazepine)	4	4
Trauma	3	3
Neoplasm (meningioma of temporal lobe and posterior fossa)	3	3
Alcoholic cerebellar degeneration	2	2
Arteriovenous malformation	2	2
Acquired immune deficiency syndrome (AIDS)	1	1
Familial paroxysmal ataxia	1	1
Viral encephalitis	1	1
Radiation	1	1
No etiology	5	5
Total		91

TABLE III: SYMPTOMS AND SIGNS IN DBN PATIENTS

	FREQUENCY (%)	NO.
Symptoms		
Dizziness, vertigo (vestibular)	44	40
Diplopia	42	38
Oscillopsia	28	25
Blurred vision	24	22
Syncope	12	11
Dysphagia	7	6
Headache	4	4
Confusion	4	4
Seizure	4	4
Signs		
Gait ataxia	64	58
Scanning speech	23	21
Limb incoordination	20	18
Hemiparesis	18	16

mean age was 30.6 years (SD, 8.6; range, 18 to 55). There was no statistically significant difference between the mean ages of the two groups of patients (Student's *t*-test, $P > .05$). The mean ages of both patient groups were significantly greater than that of the normal subjects ($P < .01$).

ETIOLOGIES

The frequencies of diagnoses in the DBN patients obtained by the neurologic examinations without the use of eye movement recordings are listed in Table II. The most common etiologies were infarction in the vertebrobasilar arterial system, cerebellar and spinocerebellar degeneration syndromes, MS, and developmental anomalies affecting the structures at the craniocervical junction and in the posterior fossa. The symptoms and signs in the DBN patients are shown in Table III. Twenty-five percent of DBN patients had infarctions. Their mean age was 63.0 years (SD, 13.4; range, 25 to 81). The disorders that were associated with infarction included arteriosclerosis, hypertension, diabetes mellitus, acute leukemia, and arteriovenous malformations. The 25-year-old patient (patient 12) was believed to have infarctions in the cerebellum and pons due to abuse of amphetamines. In most patients with infarctions, CT scans did not demonstrate the lesions. MRI studies that can demonstrate small infarcts were not available at our institution when most of the patients were studied. A typical case history of a patient with an infarction is presented.

Infarction

(Case History)—Two years ago a 72-year-old man (patient 16) developed focal seizures of the left arm and leg that were occasionally associated with loss of consciousness. Noninvasive studies of the extracranial circulation demonstrated stenosis of the right internal carotid artery. A CT scan revealed a small area of decreased intensity in the right parietal region, which was interpreted as an infarction. Cerebral angiography revealed greater than 50% stenosis of the right internal carotid artery and stenosis of the left internal carotid artery. The vertebral arteries in the neck were not stenotic. An electroencephalogram (EEG) showed abnormal activity in the right frontoparietal area. One and one-half years ago treatment with phenytoin was begun and a right carotid endarterectomy was performed. Focal seizures persisted and unsteadiness of gait developed suddenly. Scanning speech and widely based gait were found. A cerebral angiogram revealed total occlusion of the right internal carotid artery. Seizures continued despite treatment with dipyridamole and phenytoin. He was able to walk without a cane with slight ataxia of gait. One year ago nystagmus was not observed during a hospitalization, and phenytoin, primidone, and warfarin were used. At that time a left carotid endarterectomy and a right superficial temporal artery-middle

cerebral artery bypass were performed. The patient's symptoms did not improve. Six months ago DBN was observed. The patient developed blurring of vision and vertical oscillopsia. The phenytoin levels in the blood were found to be within the therapeutic range on several occasions. Discontinuation of phenytoin did not affect the ataxia or nystagmus on two occasions.

On examination at our institution the patient could not stand or walk without support. Neurologic examination revealed moderately severe dysmetria of upper and lower extremities, mild truncal ataxia, a positive Romberg sign, and an inability to walk without a widely based gait and support. Eye movement recordings are shown in Fig 1. Horizontal, square-wave jerks were present with fixation of the small laser target in center gaze, upgaze, and down gaze. They were also found in the dark. DBN was present in center gaze. Its amplitude, frequency, and slow-component velocity decreased in upgaze. The amplitude and slow-component velocity increased in down gaze, right gaze, and left gaze. Horizontal gaze-evoked nystagmus was found during gaze to the right and left. The DBN persisted

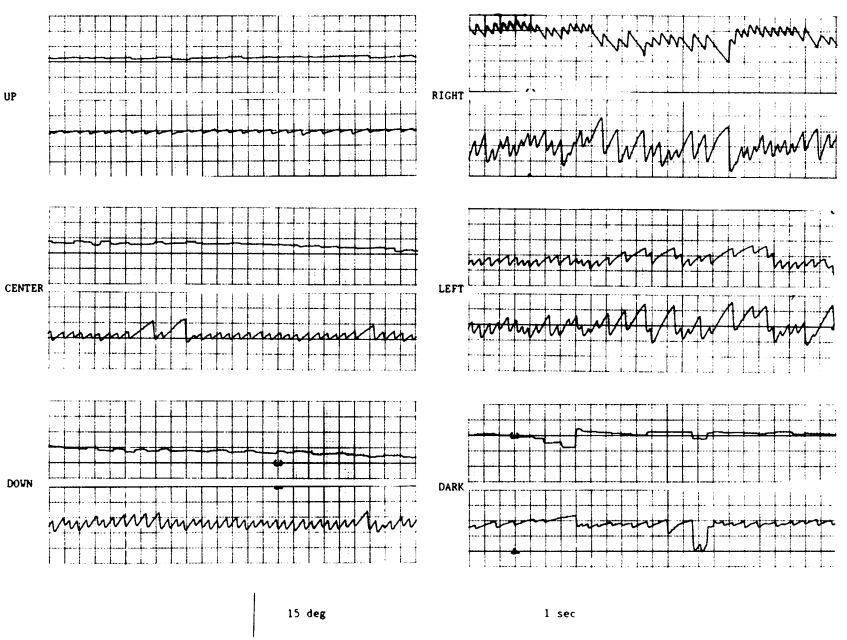


FIGURE 1

Nystagmus in patient 16. Recordings were made with magnetic search coil. Upper tracing in each pair shows horizontal eye position (deflections upward are to the right, downward are to the left); lower tracing shows vertical position (deflections upward are up, downward are down). Note horizontal, square-wave jerks in center gaze, upgaze, and down gaze and with eyes opened in the dark. DBN is present in center gaze and increased in down gaze, right gaze, and left gaze. Horizontal, gaze-evoked nystagmus is found in right gaze and left gaze.

in the dark. Horizontal smooth pursuit and OKN were severely impaired. Horizontal VOR during rotation in the dark was slightly decreased. Fixation did not inhibit the VOR normally.

The patient was believed to have suffered from an infarction of the cerebellum secondary to arteriosclerosis affecting the basilar artery. The complaint of blurred vision could have been due to the saccadic instability and DBN. Visual acuity is usually normal in patients with square-wave jerks, since the short intersaccadic intervals between saccades are long enough to permit fixation of targets with the fovea. However, the inability to refixate targets accurately with saccades can impair the ability to read. The movement of images on the retina (retinal slip) caused by the slow component of DBN does not allow sufficient time for foveation and can decrease visual acuity. The vertical oscillopsia was produced by the DBN.

Cerebellar and Spinocerebellar Degenerations

Twenty-four percent of DBN patients had cerebellar or spinocerebellar degeneration syndromes, including hereditary forms of isolated cerebellar atrophy; sporadic forms of idiopathic, isolated cerebellar atrophy; sporadic, idiopathic spinocerebellar degeneration; and sporadic, idiopathic olivopontocerebellar atrophy. Their mean age was 53.2 years (SD, 17.5; range, 19 to 82).

Sporadic, Idiopathic Cerebellar Atrophy

(Case History)—A 49-year-old man (patient 43) developed mild imbalance and difficulty in walking 7 years ago. The imbalance increased gradually. Two years ago he had difficulty with fluency of his speech. One year ago he noticed that his vision blurred when he turned his head rapidly. Neurologic examination revealed scanning speech, slight dysmetria on finger-to-nose testing, prominent ataxia on heel-knee-shin testing and a broadly based gait. DBN was observed in right gaze and left gaze. It was absent in the dark. Gaze-evoked horizontal nystagmus was present in 30° of right gaze and left gaze. Rebound nystagmus was present transiently on return to center gaze from horizontal eccentric gaze. Smooth pursuit and OKN were moderately impaired. VOR to rotation was moderately decreased. VVOR was decreased. Fixation did not inhibit the VOR normally. Biochemical screening disclosed no evidence of metabolic or toxic disorders. A medical genetics consultation did not disclose evidence of a hereditary disorder. An MRI study of the posterior fossa showed atrophy of the cerebellar vermis (Fig 2).

During the next two years the patient's symptoms and signs gradually increased. Truncal ataxia increased such that he tended to fall when he leaned over a chair. Rapid turning of the head produced nausea and vertigo, and increasingly blurred vision. The deep tendon reflexes in the lower extremities increased. The patient was thought to have a sporadic form of olivopontocerebellar atrophy. Most of his symptoms and signs were probably caused by damage to the cerebellum. The decreased VOR could be caused by damage to the vestibular nerves or to the vestibular nuclei. The complaint of blurred vision when rapidly moving the head

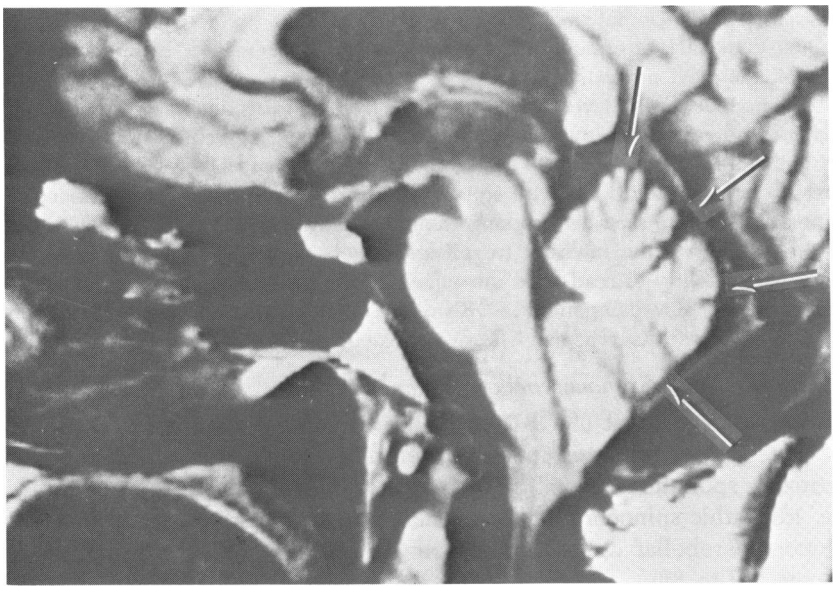
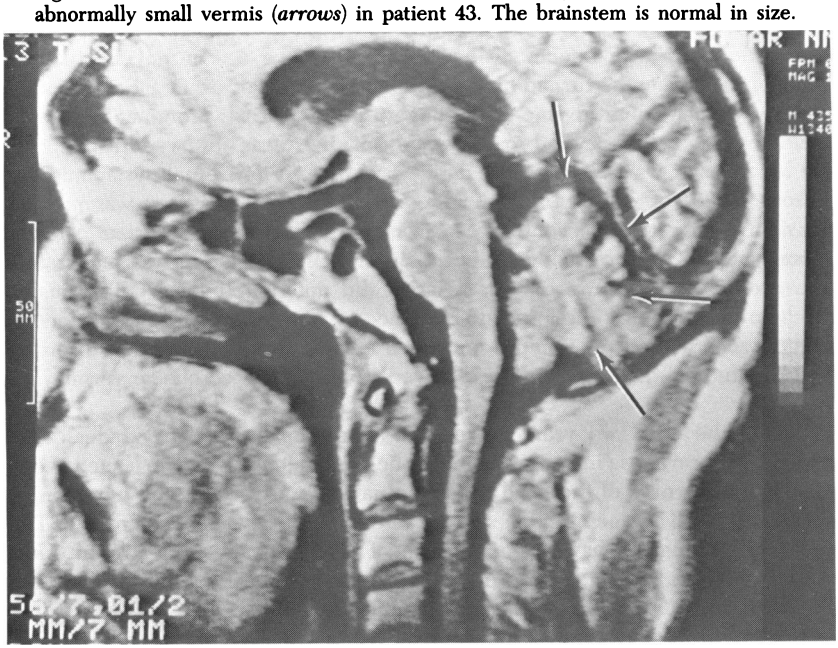


FIGURE 2

MRI scans in two patients. T-1 weighted, sagittal reconstructions. Top image shows a section through midline of cerebellar vermis, which is normal in size (*arrows*). Bottom image shows abnormally small vermis (*arrows*) in patient 43. The brainstem is normal in size.



was probably due to the decreased VOR. The VOR is primarily responsible for inducing compensatory eye movements that maintain fixation during spontaneous head movements of high frequency and velocity. In normal subjects, VOR gain is about 1 at stimulus frequencies greater than 1 Hz; the pursuit gain, in contrast, begins to decrease significantly at frequencies greater than 1 Hz. Retinal slip will occur if the VOR is impaired.

Multiple Sclerosis

Thirteen percent of DBN patients had MS. Their mean age was 43.9 years (SD, 13.3; range, 24 to 60). The patients who were 50 years of age or older, had the onset of neurologic symptoms at least 15 years earlier.

(Case History)—A 27-year-old woman (patient 46) suddenly developed loss of vision in the right eye 3 years ago. An aching pain of the right eye was present and increased with movement of the eye. Vision spontaneously returned to normal over a few months. She suddenly developed horizontal diplopia 1 year ago. Prisms in spectacles corrected the diplopia. However, it returned 6 months later in association with imbalance while walking and one episode of vertigo. She had a few episodes of incoordination of the right hand that persisted for a few seconds. On neurologic examination, there were in the right eye visual acuity of 20/30 − 3, a mild afferent pupillary defect, and slight pallor of the optic disc. In the left eye visual acuity was 20/20 and the appearance of the optic disc was normal. Gait was unaffected and the Romberg test was normal. However, the patient could not walk in tandem. She could execute rapid alternating movements of all extremities, and had normal response on finger-to-nose testing. Muscle strength and bulk were normal. Deep tendon reflexes were generally hyperactive and unsustained clonus of both ankles was found. Light touch, pin prick, and vibratory sensations were normal.

An esotropia of 25 Δ was found in center gaze and in right gaze. No tropia was present in left gaze. The ranges of all horizontal ductions were slightly decreased (40°). DBN was present in center gaze and down gaze. Upbeat nystagmus was found in upgaze. Convergence increased the amplitude of DBN in center gaze and down gaze. DBN was present in the dark looking straight ahead and to the left. Dissociated, gaze-evoked nystagmus, characteristic of bilateral internuclear ophthalmoplegia (larger amplitude of nystagmus in the abducting eyes than in the adducting eyes), was observed in right gaze and left gaze. Saccades produced by the left medial rectus, right medial rectus, and right lateral rectus was slowed. Smooth pursuit and OKN were moderately impaired. VOR to rotation was increased. VVOR was normal. Fixation did not inhibit the VOR. On examination, the CSF was unremarkable. A CT study of the posterior fossa with intravenous injection of contrast dye yielded unremarkable results.

This patient was believed to have MS. The optic atrophy of the right eye probably resulted from optic neuritis. The bilateral internuclear ophthalmoplegia was caused by lesions of the medial longitudinal fasciculi. A mild right 6th cranial nerve palsy was present. Six months later her symptoms were unchanged, but the gaze-evoked nystagmus, DBN, and upbeat nystagmus had resolved.

Developmental Anomalies

Twelve percent of DBN patients had developmental anomalies. Their mean age was 31.6 years (SD, 12.8; range, 22 to 50). The anomalies consisted of Arnold-Chiari malformations, basilar invagination, and syringobulbia.

Chiari Malformation

(Case History)—Four years ago, a 50-year-old woman (patient 63) noticed the gradual onset of dizziness when she stood up. Three years ago she developed unsteadiness of gait, blurring of vision, and oscillopsia. Relatives observed nystagmus. Her imbalance while walking gradually increased. On neurologic examination, impaired ability to make rapid tongue movements, mild ataxia on finger-to-nose and heel-knee-shin testing, widely based gait, and inability to walk in tandem were found. Marked gaze-evoked nystagmus was found in lateral gaze of 30 degrees to both sides. DBN was present in center gaze and down gaze. Its amplitude increased in horizontal gaze, with convergence, and in the dark. Square-wave jerks were also observed in center gaze, and rebound nystagmus was present on return to center gaze from horizontal gaze. Smooth pursuit and OKN were severely impaired. The VOR had abnormally high gains. VVOR was normal, but fixation suppression of the VOR was markedly impaired.

A CT study showed mild prominence of the cerebellar sulci. An MRI study of the posterior fossa revealed herniation of the cerebellar tonsils into the foramen magnum (Fig 3). A suboccipital craniotomy and laminectomy of C1 and C2 were performed. The cerebellar tonsils extended caudally to the top of the C2 lamina and the cerebellum appeared yellowish and discolored. The patient's balance, blurring of vision, and oscillopsia gradually improved. Gait and tandem walking were nearly normal. Serial eye movement recordings over the next two years demonstrated resolution of the DBN, square-wave jerks, upbeat nystagmus, and rebound nystagmus. A gaze-evoked nystagmus persisted in 40° of left gaze. Smooth pursuit, OKN, and VORfix improved. This patient had an Arnold-Chiari malformation that first produced symptoms in adulthood. Some of the damage to the cerebellum was reversible.

Other Etiologies

Four patients (4%) were thought to have toxicity from anticonvulsants (phenytoin and carbamazepine) that caused DBN. Their symptoms and DBN decreased when the medications were stopped or decreased. Other diagnoses included trauma to the brainstem and cerebellum during closed head injuries (3%), neoplasms (meningiomas of the temporal lobe and posterior fossa, 3%), alcoholic cerebellar degeneration (2%), arteriovenous malformations in the posterior fossa (2%), acquired immune deficiency syndrome (AIDS, 1%), familial paroxysmal ataxia (1%), viral encephalitis (1%), and radiation injury to the brainstem and cerebellum after irradiation of a nasopharyngeal carcinoma (1%). For five patients

(5%), the records did not contain enough information to enable an etiology to be identified.

LOCALIZATION OF LESIONS BY NEUROLOGIC EXAMINATION

The DBN patients' symptoms, signs, and laboratory tests were used to identify the anatomic locations of their lesions. The results of the quantitative eye movement studies were not used. However, internuclear ophthalmoplegia, cranial nerve palsies, and supranuclear gaze palsies that were evident during the routine neurologic examination were used. Several of the most common signs (Table III), ie, gait ataxia (64%), scanning speech (23%), and incoordination of the limbs or limb ataxia (20%), are characteristic of cerebellar dysfunction. The most frequent symptom, ataxia of gait, is associated with damage to the cerebellar vermis, whereas incoordination of the limbs is associated with damage to the cerebellar hemispheres. Forty-four percent of patients had symptoms (ie, dizziness, disequilibrium, and vertigo) characteristic of disorders of the peripheral or central vestibular pathways. The latter pathway includes projections from the vestibular nuclei to the flocculo-nodular lobe of the cerebellum. Visual symptoms occurred frequently. Ophthalmoplegias and

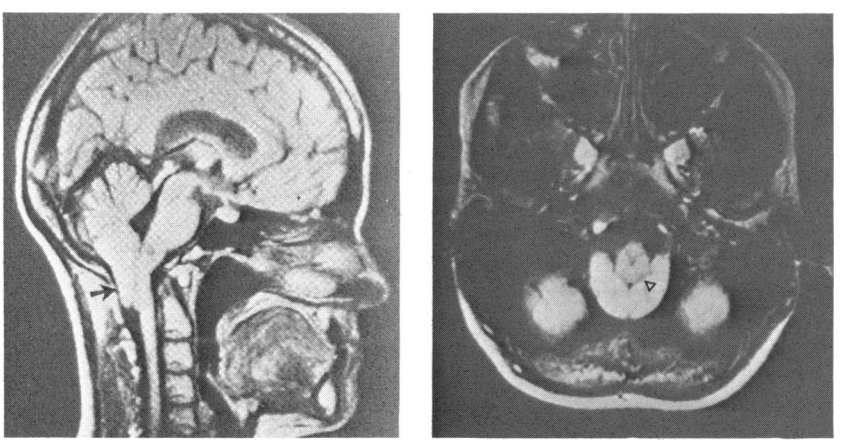


FIGURE 3

MRI scans in patients with Chiari malformations. Left scan is a sagittal, midline, T-1 weighted reconstruction in patient 63. The *black arrow* shows foramen magnum at craniocervical junction. Cerebellar tonsils have herniated into the foramen magnum. Right scan shows an axial, T-1 weighted reconstruction at the level of the foramen magnum in another patient with a Chiari malformation. The *arrowhead* points to the cervical spinal cord. Tonsils extend through the foramen magnum.

skew deviation caused diplopia (42%). Oscillopsia (28%) and blurred vision (24%) were not localizing, but were usually caused by DBN.

The locations of lesions and their frequencies are shown in Table IV. The most common locations were the cerebellum alone (49%) and the cerebellum and pons (36%). The brainstem without the cerebellum was the location in 8%. The temporal lobe or temporal lobe and cerebellum, was the location in four patients (4%) with seizures. These patients were believed to have toxicity from their anticonvulsant medications. Two patients (2%) had lesions of the midbrain, resulting from infarction and viral encephalitis. One patient had damage to the pons, medulla, and spinal cord caused by syringobulbia. Another patient with syringobulbia had localization to the medulla and spinal cord. Localization included the cerebellum in 91% of the patients.

TABLE IV: LOCALIZATION BY CLINICAL EXAMINATION IN DBN PATIENTS

LOCALIZATION	FREQUENCY (%)	NO.
Cerebellum	49	45
Cerebellum and pons	36	33
Cerebellum and midbrain	2	2
Midbrain	2	2
Pons	3	3
Pons, medulla, and spinal cord	1	1
Medulla and spinal cord	1	1
Temporal lobe	3	3
Temporal lobe and cerebellum	1	1
Total		91

TABLE V: PRESENCE OF DBN AND GAZE POSITIONS

GASE POSITION	FREQUENCY (%)	NO.
Center	64	58
Right or left	81	74
Up	45	41
Down	85	77

NYSTAGMUS CHARACTERISTICS

DBN was conjugate in all 91 patients and was present in the sitting position with fixation in 87 patients. Table V summarizes the frequencies of DBN in different positions of gaze with fixation. DBN was most frequently observed in down gaze (85%) and horizontal gaze (81%). It was present in center gaze in 64% of the patients, and was least common in upgaze (45%). DBN was not present with fixation, but was found only during positioning of the head and body in the dark in two patients (patients 30 and 61). DBN was found only in the dark in the sitting position in one patient (patient 59). DBN was present in the dark in the sitting position and during positioning in one patient (patient 29). The nystagmus characteristics of each DBN patient are presented in Table VI.

Effects of Horizontal Gaze

An increase in DBN in horizontal gaze as first described by Cogan and Barrows,[15] and has been thought to be characteristic of DBN caused by lesions in the cerebellum or lower brainstem. Halmagyi and colleagues[23] used this phenomenon as a criterion for entry into their study. They believed intuitively that this feature identified a specific type of DBN. However, the specificity of this phenomenon has not been studied. DBN in horizontal gaze was present in 81% of our patients in whom the effect was examined. Increase in DBN in horizontal gaze was not associated with any particular diagnosis. The frequencies of increased nystagmus in the common diagnoses were: infarction, 91%; degeneration, 73%; MS, 67%; and malformation, 73%. Comparisons of the frequency of each diagnosis and that of all of the other diagnoses by the chi-square test did not show statistically significant differences ($P > .05$).

The frequencies of increased nystagmus in horizontal gaze in the most common localizations were: cerebellum alone, 98%, and cerebellum-and-pons, 70%. The greater frequency in the group of patients with localization to the cerebellum alone, compared to the frequency of all localizations (80%), was statistically significant (chi-square test, $P < .01$). Ten patients did not have localizations to the cerebellum alone or in combination with the cerebellum. They were thought to have lesions to the brainstem, spinal cord, or temporal lobe. The frequency of increased nystagmus in horizontal gaze was 40% in these patients. This lower frequency, compared to that in all other patients, was statistically significant (chi-square test, $P < .01$).

TABLE VI: NYSTAGMUS CHARACTERISTICS IN DBN PATIENTS

PATIENT	HOR GAZE	DARK	CONVERGE	HALLPIKE	WAVEFORM	NULL	VORFIX
1	+	0	+	+	I	U	abn
2	+	0	NT	+	C	U*	abn
3	+	0	NT	NT	−	C	NT
4	+	+	+	NT	C,I	D	abn
5	+	0	NT	+	C	U	abn
6	+	−	+	0	?	U	abn
7	+	0	+	NT	I	U*	nl*
8	+	0	NT	NT	−	D	nl*
9	NA	NA	+	NT	NA	NA	abn
10	+	0	NT	+	?	C	NT
11	+	0	NT	+	I	C	abn
12	0	0	NT	NT	−	C	NT
13	+	0	+	0	−	C	abn
14	+	0	NT	−	−	D	abn
15	+	−	NT	NT	−	C,D	abn
16	+	0	0	NT	C	U	abn
17	+	NT	NT	NT	C	U	abn
18	0	NT	NT	NT	−	C	NT
19	+	NT	NT	NT	C	U*	abn
20	+	0	0	NT	I	D	abn
21	+	0	NT	NT	−	U*	abn
22	+	0	NT	NT	−	C	abn
23	+	+	0	NT	C	U*	abn
24	0	0	NT	NT	C	U	abn
25	+	+	NT	NT	C,I	U*	abn
26	+	−	NT	NT	?	U*	abn
27	+	0	NT	+	?	D	abn
28	+	−	NT	NT	C	U*	nl*
29	0	+	NT	+	?	NA	abn
30	0	0	0	+	?	NA	abn
31	+	0	+	+	?	D	abn
32	+	0	NT	NT	?	U*	abn
33	0	−	−	NT	−	D	nl*
34	0	0	NT	NT	C	C	abn
35	+	0	NT	+	C	C	abn
36	+	−	NT	+	−	C	abn
37	0	0	NT	0	?	C	NT
38	+	0	NT	0	I	C	nl*
39	+	+	NT	+	C,I	D	nl*
40	+	0	NT	+	−	D	NT
41	+	NT	NT	−	−	C	abn
42	+	0	NT	NT	?	C	abn
43	+	0	NT	NT	?	C	abn
44	+	0	NT	+	C	C	abn
45	+	−	NT	+	−	U*	nl*
46	0	+	+	NT	?	U	abn
47	+	0	0	+	?	D	abn
48	+	−	+	NT	?	U	nl*
49	+	0	NT	+	−	NA	NT
50	0	0	NT	NT	C	C	abn
51	+	+	+	NT	?	C	abn

TABLE VI: NYSTAGMUS CHARACTERISTICS IN DBN PATIENTS (CONT'D)

PATIENT	HOR GAZE	DARK	CONVERGE	HALLPIKE	WAVEFORM	NULL	VORFIX
52	+	0	NT	+	−	D	NT
53	0	0	NT	0	?	C	abn
54	+	0	0	NT	−	U	NT
55	0	0	NT	NT	−	C	abn
56	+	0	NT	NT	−	C	abn
57	+	0	+	NT	C	C	abn
58	+	+	0	+	I	U	abn
59	0	+	+	NT	?	NT	abn
60	+	0	0	+	−	U*	abn
61	0	0	NT	+	−	NA	nl*
62	+	0	+	0	?	U	abn
63	+	+	+	NT	I	U*	abn
64	0	−	NT	0	−	U*	NT
65	+	0	NT	NT	−	U*	abn
66	+	0	NT	NT	−	C	abn
67	+	NT	NT	NT	−	C	abn
68	+	NT	NT	NT	C,I	U	NT
69	+	0	+	NT	C	U*	NT
70	+	0	+	0	−	D	abn
71	0	NT	NT	0	?	C	abn
72	+	NT	NT	NT	C	D	abn
73	+	NT	NT	NT	−	U*	NT
74	+	0	NT	NT	C	C	abn
75	+	0	0	NT	C,I	U*	abn
76	+	+	NT	NT	−	C	nl*
77	+	+	+	NT	C,I	U*	abn
78	0	+	NT	NT	I	C	NT
79	+	−	NT	+	C	C	abn
80	+	0	+	NT	?	NA	abn
81	+	0	+	NT	−	U,D	abn
82	+	NT	NT	NT	−	U*	abn
83	+	0	NT	NT	C	C	nl
84	+	NT	NT	0	−	C	NT
85	0	0	0	NT	?	C	nl
86	+	0	NT	NT	C	U*	abn
87	+	−	+	+	?	C	abn
88	+	+	NT	+	C	U*	abn
89	+	−	−	NT	I	U*	abn
90	+	0	+	NT	−	D	abn
91	+	NT	NT	NT	?	U*	NT

+ = increase compared to center with fixation; − = decrease compared to center with fixation; 0 = same compared to center with fixation; NT = not tested; NA = not applicable. Slow-component waveforms in center with fixation: C = constant velocity, I = increasing velocity, ? = unable to judge waveform, − = no nystagmus in center.

Null positions: C = center, U = upgaze, U* = upgaze and obeys Alexander's law, D = downgaze.

VORfix: abn = abnormal suppression of VOR by fixation, nl = normal suppression, nl* = normal suppression with impaired pursuit and abnormally low VOR.

Frequency, Amplitude, and Slow-Component Velocity

The means of frequency, amplitude, and slow-component velocity of DBN are shown in Table VII. The mean values of all parameters increased in horizontal gaze compared with center gaze, although the differences in the means were significant only for frequency and velocity in left gaze (Student's *t*-test, $P = .05$). The amplitude or velocity increased in horizontal gaze in 71% (right) to 77% (left) of the patients. The frequency increased in 36% (right) to 43% (left). One or more of the parameters decreased in only 10% to 14%.

Upgaze was associated with a decrease in amplitude and velocity. The difference in mean amplitude between center and upgaze was statistically significant. Amplitude and velocity decreased in 73% of patients, and frequency decreased in 59%. These parameters increased in only 9%. The mean amplitude and frequency increased in down gaze, but the differences between down gaze and center gaze were not statistically significant. Frequency increased in 19% of patients, amplitude in 42%, and velocity in 71%. Frequency decreased in 19%, amplitude in 19%, and velocity in 24%.

Slow-Component Waveforms

Various waveforms of the slow component have been found in DBN. Zee and colleagues[19] presented recordings of nystagmus in two patients who had slow components with constant velocities. Halmagyi and co-workers[23] found constant-velocity waveforms in all 38 patients whose nystagmus was

TABLE VII: DBN AND GAZE POSITIONS

GAZE POSITION	FREQUENCY	AMPLITUDE	VELOCITY	WAVEFORM (%)				
				C	I	D	C/I	?
Center	2.6	2.7	6.6	34	16	0	10	40
1 SD	(0.6)	(1.4)	(5.5)					
Range	[2–4]	[1–6]	[1–21]					
Right	2.7	3.5	11.3	30	28	2	10	30
1 SD	(0.7)	(2.4)	(14.4)					
Range	[1–4]	[1–12]	[1–80]					
Left	3.0	3.4	12.3	30	22	0	8	40
1 SD	(0.8)	(2.2)	(13.3)					
Range	[2–5]	[1–10]	[1–60]					
Up	2.6	1.9	4.9	44	17	0	5	34
1 SD	(1.1)	(1.2)	(4.8)					
Range	[1–4]	[1–4]	[1–16]					
Down	2.5	3.5	8.6	36	11	2	1	50

C = contant velocity, I = increasing velocity, D = decreasing velocity, ? = unable to evaluate waveform.

recorded. Zee et al[43] described a patient who had slow components with exponentially increasing velocity. Lavin and colleagues[44] described a patient who had waveforms with increasing velocity (pseudocycloid). Traccis et al[45] reported that the waveforms varied from beat to beat between increasing and decreasing velocities in one patient. We observed waveforms in each position of gaze. Examples of constant-velocity, increasing-velocity, and decreasing-velocity waveforms are shown in Fig 4. Constant velocity slow components have linear or straight trajectories. Slow components with increasing velocity have curved shapes whose convexities are downward. The convexities of slow components with decreasing velocity are upward.

In 25% of patients the waveform could not be adequately classified because of noise in the eye position channel and/or very low velocities (Table VII). The most common waveform in center gaze with fixation was the constant velocity form. Among the 37 patients who had DBN in center gaze with fixation and whose waveforms could be classified, 70% had constant-velocity, 43% had increasing-velocity, and no patients had decreasing-velocity forms. Eccentric gaze had little effect on the frequency of the waveforms, except that the decreasing-velocity waveform was found only in eccentric gaze. Waveforms varied between constant velocity and increasing velocity in the same position of gaze in six patients with center gaze (16%). A change in gaze was associated with a change in waveform in the same patient in 6%.

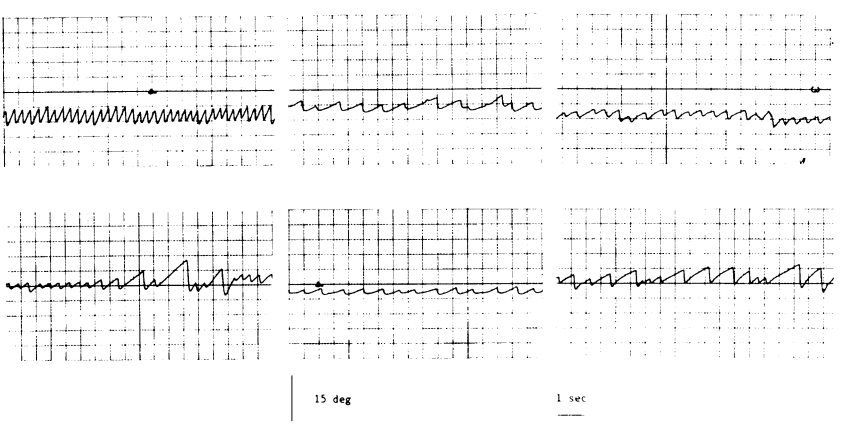


FIGURE 4

Waveforms of slow components in DBN. Recordings of vertical eye position were made with the magnetic search coil. Left column shows slow components from two patients who have linear trajectories with constant velocity; middle column shows examples of curved trajectories with increasing velocity; right column demonstrates curved trajectories with decreasing velocity.

The slow-component waveforms were not preferentially associated with particular etiologies or localizations. In etiologies with more than three observations, the frequencies in center gaze were: infarction, 64% constant and 45% increasing; degeneration, 70% constant and 30% increasing. (The total frequency in infarction is more than 100% since some patients had both constant and increasing waveforms in center gaze.) In localizations with more than three observations, the frequencies in center gaze were: cerebellum alone, 58% constant and 48% increasing; cerebellum and pons, 75% constant and 25% increasing.

Nystagmus Patterns in Vertical Gaze

The effects of vertical gaze on DBN were variable, as shown in Table VIII. Observations of the effects of eccentric gaze can be of value in identifying the etiology and in developing hypotheses about the mechanism of some forms of nystagmus. For example, in horizontal gaze-evoked nystagmus, oscillations are not present in center gaze and are induced by horizontal eccentric gaze. The slow component is in the direction toward the center of the orbit and has a trajectory with decreasing velocity.[46] Dysfunction of neural gaze-holding mechanisms, likened to "leaking" of an integrator, is though to be present. Dysfunction of neural integrators for vertical gaze-holding does not appear to be the only or primary abnormality in most patients with DBN. The pattern of nystagmus that is consistent with vertical gaze-evoked nystagmus (no nystagmus in center, upbeat nystagmus in upgaze, and DBN in down gaze) was found in only 13% of patients. Only one of these patients had a trajectory with decreasing velocity in down gaze.

An imbalance of opposing tonic innervation can produce nystagmus. For example, acute damage to and decreased innervation from semicircular canals or the vestibular nerve on one side produces spontaneous vestibular nystagmus in the horizontal plane. Baloh and Spooner[22] proposed that an imbalance in tonic vertical vestibular innervation produced DBN. An inhibitory feedback pathway in the flocculus to the anterior semicircular canal-ocular pathways might be interrupted by lesions in the cerebellum. An upward movement of the eyes (slow component) might be produced. Eccentric gaze has a consistent effect on vestibular nystagmus (Alexander's law).[47] Gaze in the direction of the fast component increases the nystagmus, whereas gaze in the opposite direction decreases it. If an imbalance in tonic vertical innervation was the cause of DBN, upgaze would be expected to decrease the nystagmus and down gaze to increase it. The frequency, amplitude and/or slow-component velocity in eccentric vertical gaze were compared to those characteristics in center gaze.

TABLE VIII: FREQUENCY (%) OF VERTICAL GAZE EFFECTS ON DBN

GAZE		GAZE		GAZE		GAZE		GAZE		GAZE		GAZE	
Up	D	Up	D	Up	D	Up	−	Up	−	Up	−	Up	+
Center	+	Center	+	Center	+	Center	+	Center	+	Center	+	Center	+
Down	I	Down	D	Down	+	Down	I	Down	+	Down	−	Down	I
14%		2%		2%		10%		3%		2%		9%	
Up	+	Up	+	Up	U	Up	U	Up	U	Up	U	Up	U
Center	+	Center	+	Center	+	Center	+	Center	+	Center	+	Center	−
Down	D	Down	+	Down	I	Down	D	Down	+	Down	−	Down	+
2%		1%		2%		2%		2%		1%		13%	
Up	+	Up	+	Up	U	Up	I	Up	I	Up	−	Up	−
Center	−	Center	−	Center	+	Center	+	Center	+	Center	−	Center	−
Down	+	Down	−	Down	D	Down	+	Down	−	Down	+	Down	−
1%		2%		7%		1%		1%		18%		5%	

+ = DBN present, − = DBN not present, I = DBN present, increased, D = DBN present, decreased, U = upbeat nystagmus present.

Twenty-seven percent of patients who were tested in vertical gaze had patterns consistent with Alexander's law (DBN decreased in upgaze, present in center gaze, and increased in down gaze; DBN absent in upgaze, present in center gaze, and increased in down gaze). In 7%, opposite effects were found (ie, upgaze increased DBN and down gaze decreased DBN). Eccentric gaze had no effects in 1%. The diagnosis of MS appeared to be associated with a low frequency of the Alexander's law pattern. None of the 11 patients with MS who had DBN in center gaze had this pattern. The remaining patient with MS had DBN only during positioning in the dark. The frequencies of the pattern in the other common diagnoses were: infarction, 23%; degeneration, 25%; and malformation, 44%. The lower frequency in MS compared to that in all other diagnoses, was statistically significant (chi-square, $P = .03$). There did not appear to be an association between the Alexander's law pattern and any particular localization. The frequencies in localizations with at least three observations were: cerebellum, 33%; cerebellum and pons, 21%; pons, 33%; and temporal lobe, 33%.

The null position is a gaze position in which nystagmus is absent or least intense. It is often found in patients with congenital nystagmus and can be significant in the treatment of this disorder. Extraocular muscle surgery, as described by Kestenbaum and others,[48,49] can move an eccentric null position toward center gaze and improve visual function.[50] In DBN oscillopsia is most disturbing in center and down gaze (reading). We have performed Kestenbaum-type surgery in three patients (patients 5, 16, and 17) who had null positions in upgaze. We were able to move the null position downward and improve visual function in center and down gaze in two of the patients (patients 5 and 17). The null position was in center gaze in 42%, in upgaze in 42%, and in down gaze in 19% of patients who had DBN with fixation in center, up, or down gaze. Null positions were found in two of the three gaze positions in two patients.

The frequency of a null position in upgaze was greater in patients with malformations than in patients with the other common diagnoses. The frequencies were 78% in malformations, 45% in infarctions, 27% in MS, and 30% in degenerations. The difference between the frequency in malformations and those in all other diagnoses was statistically significant (chi-square, $P = .02$). There was no association between frequencies of null positions in upgaze and the localizations. The frequencies of null positions in down gaze and center gaze were not significantly different among the various diagnoses and localizations.

Effects of Convergence, Dark, and Positional Testing

Convergence has been reported to increase DBN in some patients.[23,51] This observation is significant, since testing with convergence might increase the ability to detect nystagmus. Lavin and colleagues[44] described a patient in whom convergence decreased DBN. In our study, 33 patients were tested with fixation at distance and with fixation at 25 cm. Convergence increased the frequency and/or amplitude of DBN in 64%, decreased the nystagmus in 6%, and had no effect in 30% of the patients tested (Table IX). Fig 5 illustrates the effect of convergence on nystagmus in patient 63. A small-amplitude DBN was present in center gaze with fixation of a small target at 2 m. Convergence to 25 cm increased the amplitude, frequency, slow-component velocity. Convergence can transform an upbeat nystagmus into DBN. Fig 6 shows nystagmus in patient 9 fixating a small target at 1 m and at 5 cm. Upbeat nystagmus was found in center gaze, right gaze, and left gaze at distance. Convergence produced a small-amplitude, low-frequency DBN in the same positions of gaze. In 21% of patients (7 of 33), convergence produced DBN in a position in which it had not been present. In 6% (2 of 33), DBN had not been present in any gaze position with fixation at distance, but was found with convergence.

The frequencies with which convergence increased DBN were not significantly different among the common diagnoses and localizations. The frequencies were infarctions, 67%; MS, 67%; and malformations, 60%. The frequency in degenerations was only 33%. However, only three patients with this diagnosis were tested, and the difference in frequency, compared with that in all other diagnoses, was not statistically significant (chi-square, $P > .05$). The frequencies among common localizations were cerebellum alone, 78%, and cerebellum-and-pons, 71%.

Blockage of fixation by placing patients in the dark with eyes opened characteristically increases the amplitude and slow component velocity of vestibular nystagmus,[52] since fixation suppresses the nystagmus. Lack of suppression indicates the presence of damage to the brainstem and/or cerebellum. DBN was sought in the sitting position in the dark in 78 patients and was compared to DBN with fixation (Table IX). Blockage of fixation increased DBN in 18% of the patients. DBN was decreased in 15%. No effect was found in 67%. The frequencies of increased nystagmus among the common diagnoses were infarctions, 11%; degenerations, 14%; MS, 17%; and malformations, 33%. The differences among the diagnoses were not statistically significant (chi-square, $P > .05$) The frequencies of increased nystagmus in the common localizations were cerebellum alone, 18%, and cerebellum-and-pons, 17%.

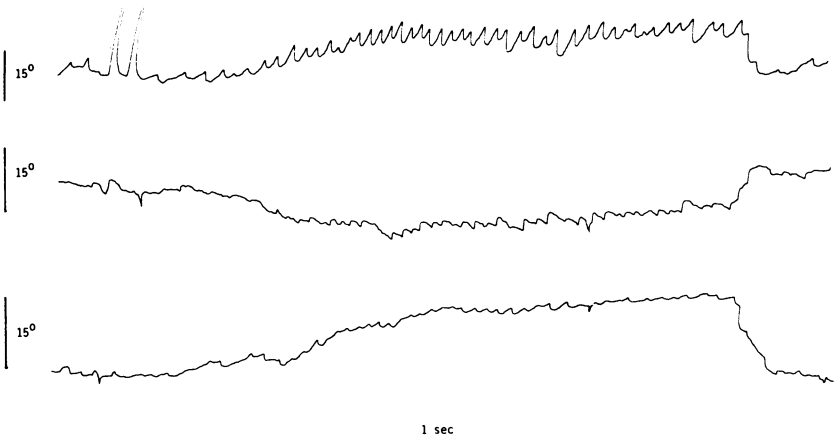


FIGURE 5
Effect of convergence on DBN. Recordings were made with EOG in patient 63. Upper tracing shows the vertical position of left eye; middle tracing shows horizontal position of right eye; lower tracing shows horizontal position of left eye. Two artifacts from eyelid blinks are present before convergence begins. Convergence from 2 m to 25 cm increases the amplitude, frequency, and slow-component velocity of DBN.

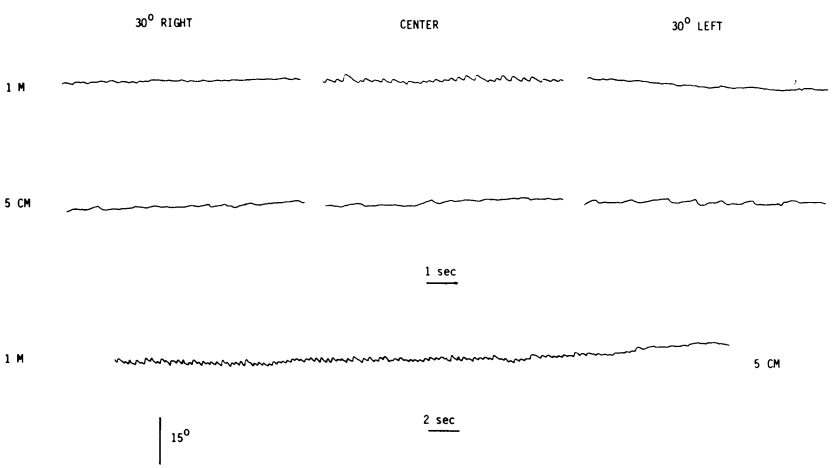


FIGURE 6
Effect of convergence on DBN. Recordings were made with EOG in patient 9. Fixation at 1 m (top tracings) produces an upbeat nystagmus in center gaze, right gaze, and left gaze. Fixation at 5 cm (middle tracing) transforms the nystagmus into DBN. Gradual convergence from 1 m to 5 cm decreases the amplitude of the upbeat nystagmus.

TABLE IX: EFFECTS OF CONVERGENCE, DARKNESS, AND POSITIONING ON DBN

MANEUVER	FREQUENCY (%)	NO.
Convergence[1]		
Increase	64	21
Decrease	6	2
No effect	30	10
Total	100	33
Darkness[2]		
Increase	18	14
Decrease	15	12
No effect	67	52
Total	100	78
Positional testing[3]		
Absent	30	11
Static position	39	14
Hallpike maneuver		
Increase	67	24
Decrease	28	10
No effect	6	2

1 = effect of convergence to 0.25 m compared to fixation at 2 m.
2 = effect of darkness in sitting position compared to fixation.
3 = effect of positioning compared to sitting upright with fixation (36 patients tested, total is not 100%).

Chambers and colleagues[53] reported that static tilt away from the upright position and linear accelerations induced DBN in one patient. They suggested that a lesion of the cerebellar nodulus could damage an inhibitory influence on otolith-ocular responses, causing DBN. However, the effects of tilt on dynamic vertical canal-ocular responses were not tested in this patient. Gresty and co-workers[54] studied these effects in two patients. They concluded that the primary abnormality in DBN was an asymmetry of vertical canal-ocular responses that was modulated by otolith stimulation in some patients and was insensitive to tilt in others.

Positional testing in the dark was performed in 36 patients in our study. Fig 7 demonstrates positional testing in patient 39. A DBN of very low amplitude and low slow-component velocity was present in center gaze and right gaze. The frequency and velocity increased in left gaze and upgaze. DBN was absent in down gaze. The amplitude of DBN increased while the patient was seated in the dark and instructed to look straight

ahead, to the right, and to the left. Hallpike maneuvers with the head hanging to the right and to the left increased the amplitude and slow-component velocity for several seconds. A DBN with low frequency, amplitude, and velocity was found in the dark in the supine positions and lateral positions. A DBN of larger amplitude and velocity was present in the supine position with the head turned to the left. The nystagmus persisted as long as this position was maintained.

Nystagmus was not present during positional testing in 30% of the patients tested (Table IX). DBN was found during static positioning in 39%. Two patients (patients 30 and 61) had DBN during positional testing but did not have DBN in the sitting position in the light or in the dark. Among the patients with DBN during positional testing, DBN was equally prevalent in the supine, the supine-head right or left, and the right or left

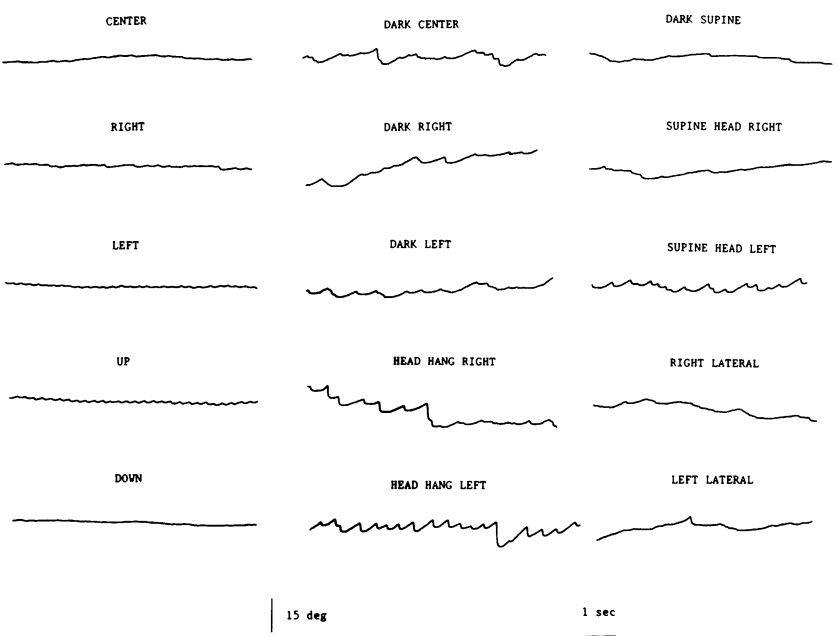


FIGURE 7

Effects of positional testing on DBN. Recordings of vertical eye position were made with EOG in patient 39. A low-amplitude DBN is present in center gaze and right gaze while the patient was fixating a small target. It increased in left gaze and upgaze. The amplitude increased while the patient was seated with eyes opened in the dark. Hallpike maneuvers transiently increased the nystagmus. The supine and lateral positions did not affect DBN, except for the supine head left position, which increased the nystagmus.

lateral positions (17% to 22%). The Hallpike maneuver increased the amplitude of DBN in 67% of the patients tested. It decreased the amplitude in 6% and had no effect in 27%. The frequencies with which the Hallpike maneuver increased DBN among the common diagnoses were: infarctions, 63%; degenerations, 77%; MS, 75%; and malformations, 60%. The frequencies in the common localizations were: cerebellum, 68, and cerebellum-and-pons, 71%. The differences in frequencies among the diagnoses and localizations were not statistically significant (chi-square, $P > .05$).

ANALYSIS OF EYE MOVEMENT RECORDINGS

Group Means in Normal Subjects, DBN Patients, and Cerebellar Atrophy Patients

Quantitative parametric studies of saccades, smooth pursuit, OKN, VOR, and visual-vestibular interactions from our laboratories have been published previously.[32,33,35,42,55-57] The eye movements in normal subjects measured in the present study were similar to those that we have reported earlier. The means of measurements from our groups of normal subjects, patients with DBN, and patients with cerebellar atrophy who did not have DBN are presented in Tables X and XI.

Smooth pursuit, OKN, and of VORfix were impaired in both groups of patients, compared to those eye movements in normal subjects. The gains of smooth pursuit and OKN were abnormally low in the patients, indicating that their eye movements could not match the velocity of the targets. The gains of VORfix were abnormally high, demonstrating that the patients could not normally inhibit vestibular nystagmus produced by rotation. The differences in mean gains between the patient groups and the normal subjects were statistically significant (Student's t-test, $P < .05$). From 79% to 97% of the DBN patients tested had smooth pursuit and OKN gains below the range of values in the normal subjects. From 75% to 100% of patients with cerebellar atrophy had smooth pursuit and OKN gains below the normal range. All of the patients with cerebellar atrophy had VORfix gains above the normal range, whereas 53% to 66% of patients with DBN had VORfix gains above the normal range. As indicated in Table I, the DBN patients with normal values of VORfix gain had abnormally low VOR gain.

VOR to rotation in the dark were generally similar in both groups of patients and the normal subjects. The gain of VOR in the DBN patients when they were rotated at 0.05 Hz was slightly, but significantly, lower than that in normal subjects ($P < .01$). The frequencies of outliers (values above or below the normal range) in this test were similar in both patient

TABLE X: GAINS OF PURSUIT AND OKN IN NORMAL SUBJECTS, DBN PATIENTS, AND CEREBELLAR ATROPHY PATIENTS

	PURSUIT[1]			OKN[2]		
	0.1 Hz	0.2 Hz	0.4 Hz	CONSTANT	0.2 Hz	0.05 Hz
Normal subjects (n = 19)						
Mean	.99	.98	.90	.90	.88	.86
1 SD	.04	.05	.04	.10	.08	.11
Range	.90–1.00	.84–1.00	.84–.95	.70–1.00	.74–.99	.74–1.00
NL *vs* DBN	+	+	+	+	+	+
NL *vs* CA	+	+	+	+	+	+
DBN patients (n = 72)						
Mean	.69	.58	.44	.49	.56	.22
1 SD	.24	.28	.27	.21	.24	.22
Range	.21–1.00	0–1.00	0–.91	.08–.93	.09–.94	0–.95
Outliers (%)	79	76	97	88	80	94
DBN *vs* CA	–	–	+	–	–	–
Cerebellar atrophy patients (n = 11)						
Mean	.77	.51	.28	.48	.46	.16
1 SD	.16	.24	.12	.17	.23	.12
Range	.55–.91	.10–.86	.09–.53	.21–.70	.15–.83	.05–.39
Outliers (%)	75	91	100	82	80	100

1 = target motions of 0.1 Hz, 0.2 Hz, and 0.4 Hz.
2 = OKN drum motions of 30°/sec constant, 0.2 Hz and 0.05 Hz.
SD = standard deviation.
Outliers = values below range of normal subjects.
+ = differences in means, $P \leq .05$ (Student's *t*-test).
– = differences in means, $P > .05$ (Student's *t*-test).

TABLE XI: GAINS OF VOR, VVOR AND VORFIX IN NORMAL SUBJECTS AND PATIENTS

	VOR[1]		VVOR		VORFIX	
	0.2 Hz	0.05 Hz	0.2 Hz	0.05 Hz	0.2 Hz	0.05 Hz
Normal subjects (n = 19)						
Mean	.52	.61	.97	.99	.02	.02
1 SD	.16	.14	.07	.07	.02	.02
Range	.31–.81	.39–.91	.81–1.02	.88–1.10	0–.06	0–.10
NL *vs* DBN	–	+	+	+	+	+
NL *vs* CA	–	–	–	–	+	+
DBN patients (n = 72)						
Mean	.52	.47	.92	.81	.22	.23
1 SD	.26	.24	.17	.23	.24	.24
Range	.13–1.07	.03–1.07	.42–1.31	.16–1.12	0–1.03	0–.95
Outliers (%)	40	42	85	58	66	53
	30–	36–	75–	55–		
	10+	6+	10+	3+		
DBN *vs* CA	–	–	–	–	+	–
Cerebellar atrophy patients (n = 11)						
Mean	.70	.50	.86	.88	.40	.45
1 SD	.33	.24	.33	.19	.23	.26
Range	.10–1.34	.05–.95	.65–1.37	.61–1.10	.17–.91	.20–.95
Outliers (%)	9–	30–	10–	45–	100	100
	36+	1+	40+	0+		

1 = chair motions of 0.2 Hz and 22.6°/sec, 0.05 Hz and 60°/sec.
SD = standard deviation.
Outliers = above (+) or below (−) range of normal subjects.
+ = differences in means, $P \leq .05$ (Student's *t*-test).
− = differences in means, $P > .05$ (Student's *t*-test).

groups. The mean gains of synergistic VVOR were slightly lower in both patient groups than in the normal subjects. However, only the differences in the DBN patients were statistically significant ($P = .05$ at 0.2 Hz; $P < .01$ at 0.05 Hz).

The patterns of abnormal eye movements (abnormally low smooth pursuit and OKN gains and abnormally high VORfix gains) were the same in DBN patients and cerebellar atrophy patients. The differences in mean gains between the groups of patients were not statistically significant ($P > .05$) with one exception. The VORfix at 0.2 Hz in DBN patients was significantly less than that in cerebellar atrophy patients ($P = .01$).

Localization of Lesions in DBN Patients by Eye Movement Recordings

Gain values in the eye movement tests were considered to be abnormal if they were beyond 2 SD from the group mean values of normal subjects established in the parametric studies. Localization to the cerebellum was made by identification of a characteristic pattern of abnormalities in horizontal eye movements. The pattern consisted of decreased gain of smooth pursuit, decreased gain of OKN, and increased gain of VORfix.[20,32-35] Eye movements of a normal subject are shown in Fig 8. Note

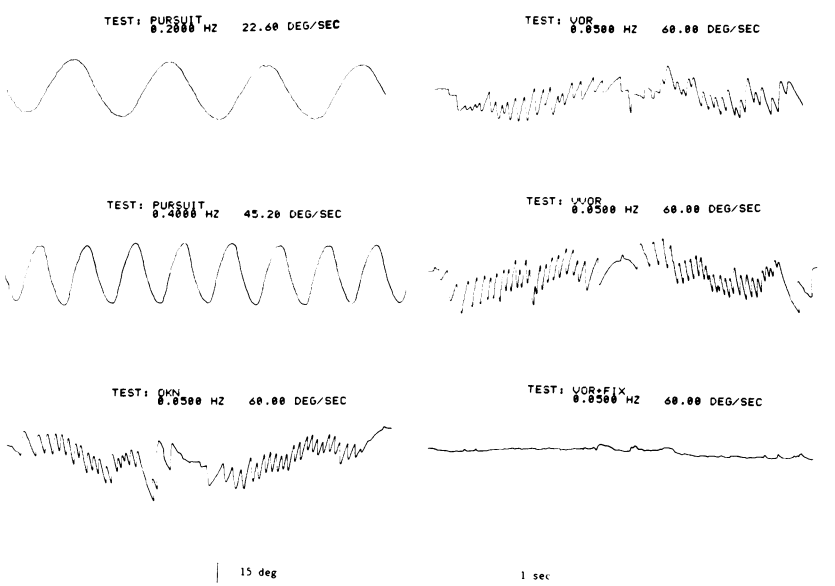


FIGURE 8

Eye movement systems in a normal subject. Horizontal eye position recordings were made with EOG. The frequencies and peak velocities of sinusoidal stimuli are indicated under each test. Note that trajectories of pursuit are smooth and that vestibular nystagmus is almost completely inhibited by fixation during the VORfix test.

that the trajectories of the eyes during smooth pursuit tracking are smooth, indicating the presence of few catch-up saccades. The amplitude of vestibular nystagmus is increased during VVOR. Fixation during the VORfix test almost completely inhibits vestibular nystagmus. The graphs of eye velocity *vs* time and measurements of gain produced by the on-line computerized analysis system are shown in Fig 9. Most of the saccades and fast components were removed from the data. The gains of pursuit and OKN are about 1. The VORfix gain is nearly 0.

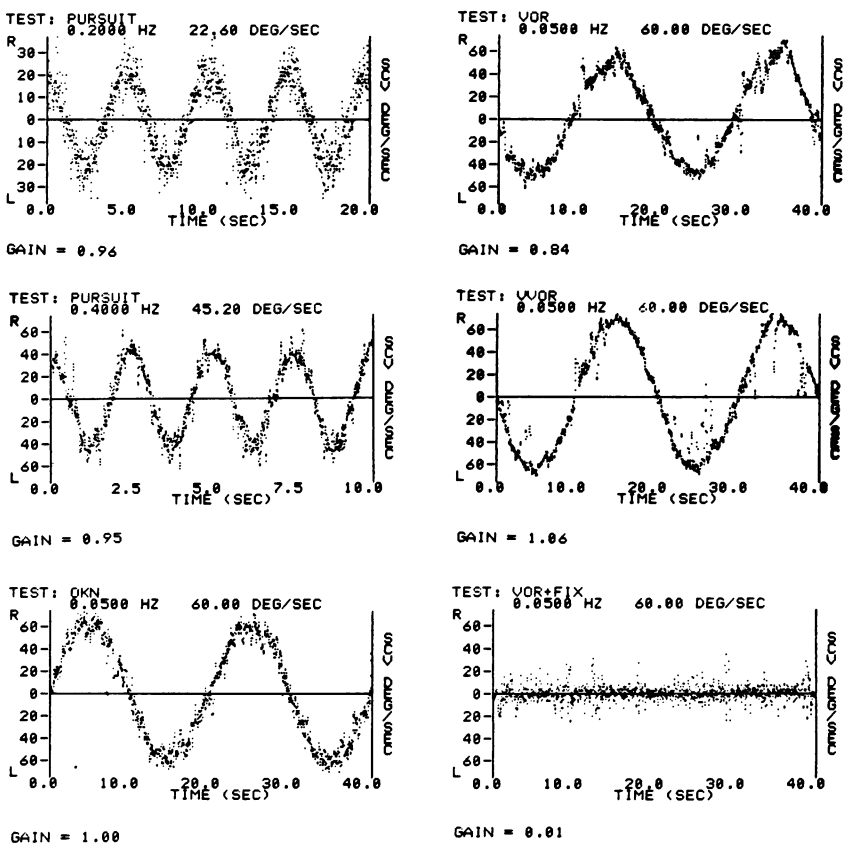


FIGURE 9

Eye movement systems in a normal subject. On-line, computerized analyses of eye velocity *vs* time and measurements of gain from the subject in Fig 8 are shown. The frequencies and peak velocities of the sinusoidal stimuli are shown under each test. Note that fixation almost completely inhibits vestibular nystagmus in the VORfix test and that the gain is nearly 0.

An example of the cerebellar pattern in a patient with DBN (patient 32) is shown in Fig 10. Note that during smooth pursuit the eye falls behind the target and large-amplitude catch-up saccades are made. The amplitude and slow-component velocity of OKN are less than in normal subjects. The VOR is normal. The amplitude and velocity of vestibular nystagmus are increased in the VVOR test. However, fixation cannot suppress vestibular nystagmus during the VORfix test. Graphs of eye velocity *vs* time and measurements of gain are shown in Fig 11. The gains of pursuit and OKN were abnormally low. The gain of VORfix was abnormally high.

The pursuit system has been thought to be responsible for suppression of the VORfix and enhancement of the VOR during VVOR tests. Inability to suppress the VOR is usually associated with impaired pursuit and OKN, and asymmetric pursuit is associated with asymmetric suppression of the VOR.[58,59] However, some observations suggest that VOR suppression might not depend on the pursuit system.[60] Three patients with

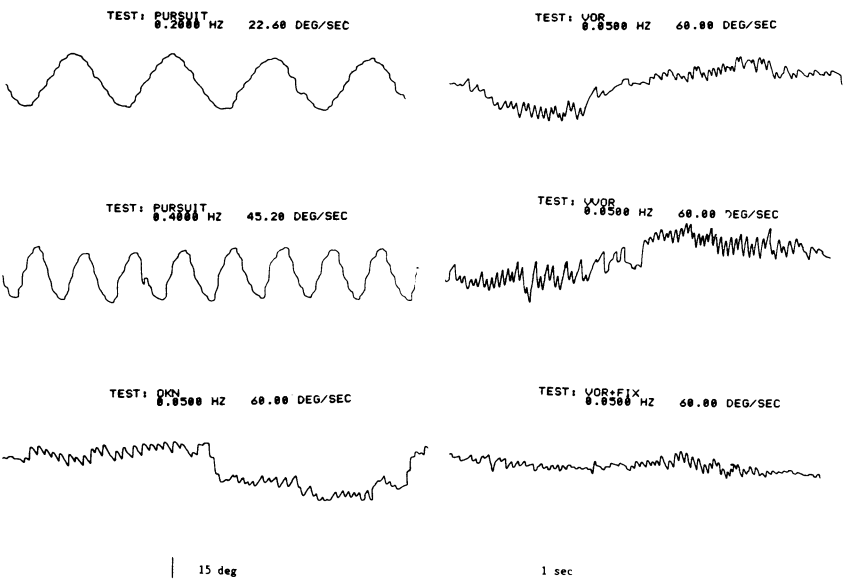


FIGURE 10

Eye movement systems in a patient with DBN and the cerebellar pattern of eye movement abnormalities. Horizontal eye position recordings were made with EOG in patient 32. The frequencies and peak velocities of sinusoidal stimuli are indicated under each test. Note that smooth pursuit cannot match the target velocity and that a series of catch-up saccades is made. Synergistic interactions of visual tracking and the VOR are able to increase the amplitude and velocity of vestibular nystagmus in the VVOR test. However, fixation cannot inhibit vestibular nystagmus in the VORfix test.

spinocerebellar degeneration have been described as having abnormal VORfix and normal pursuit,[61] but such patients are unusual. In these patients saccades were abnormally slow, making separation of smooth pursuit movements from catch-up saccades difficult. The velocity of slow saccades can be in the range of pursuit movements, and abnormal saccades can be mistaken for pursuit movements.

The gain of VORfix might not be abnormally high in some patients with cerebellar disorders and impaired pursuit and OKN. The VORfix gain can

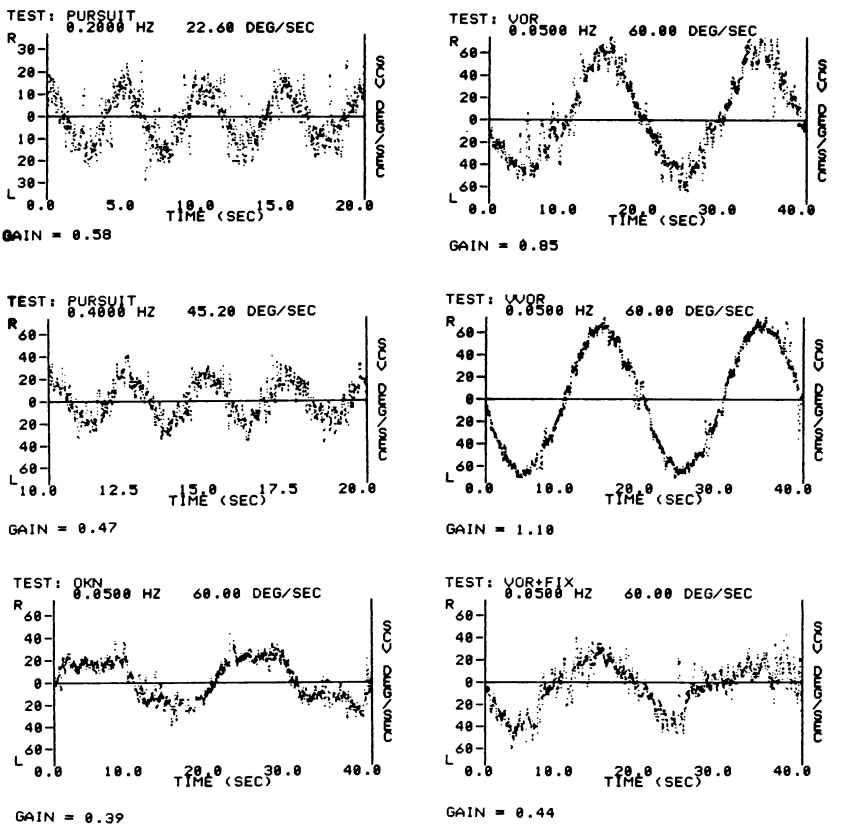


FIGURE 11

Eye movement systems in a patient with DBN and the cerebellar pattern of eye movement abnormalities. On-line, computerized analyses of eye velocity *vs* time and measurements of gain from patient 32 are shown. The frequencies and peak velocities of the sinusoidal stimuli are shown under each test. Note that the gains of pursuit and OKN are abnormally low. Fixation cannot normally inhibit vestibular nystagmus in the VORfix test, and the gain is abnormally high.

be predicted by the pursuit and VOR gains.[62,63] The VORfix gain is high if the pursuit gain is low and the VOR gain is normal. The VORfix gain is lower (less abnormal) if the pursuit gain is only slightly decreased. The VORfix gain can be normal even if the pursuit gain is low, if the VOR gain is very low. The VOR can be decreased in patients with cerebellar damage if the vestibular nerves or vestibular nuclei are also impaired, as in some patients with spinocerebellar degenerations, such as olivopontocerebellar atrophy and Friedreich's ataxia. Therefore, localization to the cerebellum was made in this study when the VORfix gain was within the normal range and the pursuit gain was abnormally decreased, if the VOR gain was more than 2 SD below the normal means (gain less than 0.20 at 0.2 Hz and less than 0.33 at 0.05 Hz).

Localization to the pons was made if abnormalities characteristic of internuclear ophthalmoplegia (slowing of adducting saccade, abducting nystagmus, and limitation of adduction)[64] were found in the presence of signs of midbrain damage, or if abnormalities characteristic of pontine paramedian reticular formation (PPRF) lesions (symmetrical slowing and hypometria of conjugate saccades)[65] were found. Localization to the midbrain was made if signs of supranuclear palsy of vertical gaze were found (limitation of voluntary gaze, increased range of versions with Bell's phenomenon and/or Doll's head maneuver, and symmetrical hypometria and/or slowing of conjugate saccades).[66]

Quantitative analyses of eye movements were sufficient to allow localization in 72 DBN patients. The data from one patient who had an intermittent DBN due to a Chiari malformation (patient 61) was excluded from the analysis.[67] She had normal horizontal eye movements, except for decreased VOR to rotation and caloric stimulation. Although her horizontal eye movements have been tested on several occasions, tests were not performed during a period of DBN.

Eighty-seven percent of DBN patients who had quantitative eye movement recordings had localizations to the cerebellum alone (Table XII). Eleven percent had eye movement abnormalities characteristic of cerebellar and pontine damage. No patient had localization to the pons alone. One patient (1%) demonstrated cerebellar and midbrain patterns. One patient (1%) had only a midbrain pattern. A total of 99% of DBN patients who had quantitative eye movement recordings demonstrated the cerebellar pattern of eye movement abnormalities.

In four patients with DBN, lesions were localized to the midbrain on the basis of their clinical examinations (Table I). Patient 74 was a 25-year-old woman who suffered a head injury in a motorcycle accident. She had vertical diplopia, gait ataxia, and scanning speech. Limitation of upgaze

TABLE XII: LOCALIZATIONS OF EYE MOVEMENT RECORDINGS IN DBN PATIENTS

LOCALIZATION	FREQUENCY (%)	NO.
Cerebellum	87	63
Cerebellum and pons	11	8
Cerebellum and midbrain	1	1
Midbrain	1	1
Total		72

and decreased velocities of upward and downward saccades were found. DBN was found in upgaze, down gaze, and horizontal gaze. Quantitative eye movement recordings showed impaired pursuit, OKN, and VORfix. Eye movement abnormalities in this patient demonstrated cerebellar and midbrain patterns. Patient 85 was a 31-year-old man who was thought to have a viral encephalitis of the brainstem. He had limitation of upgaze and decreased velocities of upward and downward saccades. A peripheral 6th cranial nerve palsy was present on the right side. DBN nystagmus was present only in down gaze. Smooth pursuit, OKN, VOR, VVOR, and VORfix tests were normal. This patient was believed to have only a midbrain pattern of abnormal eye movements.

Two other patients had localizations to the midbrain by clinical examination, but did not have quantitative eye movement recordings. Patient 18 was a 78-year-old woman with hypertension who suddenly developed vertical diplopia. Limitation of upgaze, decreased velocities of vertical saccades, and horizontal gaze-evoked nystagmus were found. DBN was present only in down gaze. Horizontal eye movement systems were not tested quantitatively. This patient was thought to have only a midbrain pattern of eye movement abnormalities. Patient 78 was a 26-year-old man who had a large meningioma in the posterior fossa. He had gradually developed vertical diplopia, oscillopsia, and ataxia of gait and limbs. He could not elevate his eyes above the midline. DBN was present only in down gaze with fixation and in center gaze in the dark. Clinical examination of eye movements showed impaired pursuit, OKN, and VORfix. However, quantitative eye movement recordings were not obtained. He was thought to have damage to the midbrain and cerebellum.

DISCUSSION

Many disorders can cause DBN. In our study, as in previous studies, the most common causes were infarction, cerebellar and spinocerebellar degeneration syndromes, MS, and developmental anomalies that affect the cerebellum and lower brainstem. These diagnoses accounted for 74% of the etiologies in our patients with DBN. The identification of etiologies was based on routine clinical examination that relied on the history of the clinical course and neuroanatomic correlations from findings in the physical examination. Several uncommon causes were also identified. For example, four of our patients were thought to have drug toxicity. In other reports DBN has been associated with phenytoin,[68,69] carbamazepine,[70,71] lithium,[72] and depletion of magnesium.[72-74] In the four patients in our study, the toxicity was believed to be due to phenytoin and carbamazepine. Quantitative eye movement recordings were made in three of the four, and in all three the cerebellar pattern of eye movement abnormalities was identified. Therefore, the neurotoxicity associated with DBN might also affect the cerebellum. Other unusual causes of DBN that were found in this study or in other reports include alcoholism,[75] viral encephalitis,[76,77] vitamin B12 deficiency,[78] nutritional deficiency due to hyperemesis gravidarum,[43] and AIDS.

The use of MRI to study the structures within and near the posterior fossa will increase our ability to identify and localize the lesions of the brainstem and cerebellum associated with DBN. Most of the infarctions and demyelination that we thought were the causes of DBN could not be demonstrated by CT scanning, but might be found by MRI. MRI was useful in identifying the developmental anomalies, such as Arnold-Chiari malformations and syringobulbia, and in demonstrating the atrophy of the cerebellum in degeneration syndromes.

DBN has several distinctive characteristics. In most patients its amplitude and velocity increase in horizontal gaze, making detection by the unaided eye easier. This phenomenon, however, is not useful in differentiating among the diagnoses associated with DBN: horizontal gaze increased DBN in 80% of the patients tested in our study. Convergence increased DBN in 64% of our patients. In some patients DBN was not present in a particular position of gaze without convergence, and in a few patients it was not found in any position of gaze without convergence. In screening therefore, for nystagmus, the stability of fixation with a target close to the patient should be tested. The reasons why horizontal gaze and convergence affect DBN are not known. It is not likely that the effect of convergence is simply due to greater difficulty in maintaining stable fixation of a near target. Convergence can cause a transformation of

upbeat nystagmus into DBN, as shown in Fig 6 and as reported previously.[79] Halmagyi and colleagues[23] described a patient in whom convergence changed DBN to upbeat nystagmus.

Positional testing in the dark can be helpful in detecting DBN. The rapid positioning of the Hallpike maneuver increased the amplitude of DBN in 65% of the patients tested. In a few of these patients, DBN was not detected in the sitting position in the dark or with a fixation target. If DBN is caused by a tonic imbalance of vertical semicircular canals or by a disturbance of the otolith system, rapid positioning would be expected to affect the nystagmus, since they are stimulated by this maneuver.

Our study of the characteristics of DBN did not disclose patterns that identified specific etiologies. With few exceptions, the frequencies of the different nystagmus characteristics were not significantly different among the diagnoses and localizations. A higher frequency of increased DBN in horizontal gaze in patients with localizations to the cerebellum alone, a lower frequency of the Alexander's law pattern in vertical gaze in patients with MS, and a higher frequency of the null position in upgaze in patients with malformations were found. The reasons for these findings are not evident. Knowledge of the effects of various maneuvers on DBN can lead to earlier detection of disorders that cause DBN, and consequently to earlier and perhaps more effective treatment.

Clonazepam has been reported recently to be effective in decreasing DBN and oscillopsia in several patients.[53,80] Quantitative measurements of nystagmus and other eye movements have been helpful in studying the effects of this treatment. Four patients in our study have been treated. The frequency, amplitude, and velocity of nystagmus were decreased in two patients after a single dose of medication and after several weeks of treatment. However, impairment of pursuit, OKN, and visual-vestibular interactions did not improve. None of the patients elected to continue treatment because of lack of subjective improvement in vision and because of side effects of drowsiness and fatigue. The most effective treatment, of course, would correct the disorder affecting the cerebellum before damage is severe and irreversible. Discontinuation of toxic drugs[72] and surgical decompression of Chiari malformations[81] have been shown to abolish DBN. The presence of a well-defined null position in upgaze and the existence of significant impairment of vision in center and down gaze due to oscillopsia were used as indications for movement of the null position by surgery on the extraocular muscles in three of our patients.

Our study of the localization of lesions by the clinical examination indicates that DBN is associated with damage to the cerebellum. In this study, 88% of DBN patients had symptoms and signs on neurologic

examination that were consistent with damage to the cerebellum. Many patients with DBN also have symptoms and signs indicating damage to the pons (36% in this study). The precision of localization from the clinical examination is limited. It is usually not possible to distinguish between lesions only in the pons that also affect pathways to the cerebellum, producing evidence of cerebellar dysfunction, and multiple lesions in the pons and cerebellum. Nevertheless, the fact that the clinical examination rarely led to localizations to structures outside of the cerebellum alone strongly suggests that the cerebellum is the primary location of lesions causing DBN. The two patients who were thought to have only damage to the midbrain are interesting exceptions and indicate that lesions in the upper brainstem can also produce DBN.

This is the first study to use quantitative eye movement studies in a large number of patients to localize the lesions associated with DBN. Of the DBN patients who were tested, 99% had eye movement abnormalities characteristic of damage to the cerebellum. The pattern of abnormalities consisted of impaired smooth pursuit, OKN, and VORfix. This pattern has been reported in other studies of patients with cerebellar disorders and in animals with experimental lesions in the cerebellar flocculonodular lobes and vermis. Most patients in our study who had lesions localized to structures outside the cerebellum by clinical examination were found to have the cerebellar pattern of eye movement abnormalities. These patients probably also had damage to the cerebellum that was responsible for the DBN. Our group of patients with cerebellar atrophy who did not have DBN had eye movement abnormalities resembling those of the patients with DBN. In general, no statistically significant differences in mean gains were found in the eye movement tests between the two patient groups. The similarity demonstrates that the abnormalities of smooth pursuit, OKN, and suppression of the VOR found in the DBN patients are not simply caused by the DBN alone. It also indicates that damage to the cerebellum might be a necessary factor for the production of DBN in most patients, but is not a sufficient factor.

What is the relationship between DBN and the abnormalities in horizontal eye movements? Medhorn and colleagues[82] studied vertical and horizontal nystagmus, pursuit, and VOR in four patients with DBN. The found abnormal horizontal responses in all of the patients and concluded that there is a close topographical and functional relationship between the cerebellar pathways for vertical movements and those for horizontal movements. The midline structures of the cerebellum (flocculi and vermis) are important in the control of horizontal movements. The lesions that produce DBN are most likely within these structures, as indicated by the high frequency (99%) of horizontal abnormalities in our patients with

DBN. However, the pathways in which damage produces DBN and those in which impairment causes abnormal horizontal pursuit, OKN, and visual-vestibular interactions are clearly not identical. Four hundred forty-one patients who were studied in our laboratories were found to have a cerebellar pattern of horizontal eye movement abnormalities during the 10-year period of this study. Only 21% of these patients had DBN. We attempted to demonstrate a relationship between parameters of DBN and the abnormalities in horizontal eye movement. For example, the slow-component velocity of DBN in center gaze was compared to the gain of horizontal pursuit and to the gain of horizontal VORfix, using linear regression and bivariate curve fitting models. No statistically significant correlations were found.

Several mechanisms have been proposed for DBN. A defect in transmission of visual input about downward velocity to a neural integrator for vertical smooth movements might produce a tonic imbalance in the pursuit system.[19,75] Upward slow components of DBN would have trajectories with constant velocities. Upward pursuit would be better than downward pursuit. Zee and colleagues suggested that patients who have slow components with decreasing-velocity trajectories might have leakiness of a neural integrator in the brainstem resulting from cerebellar dysfunction,[43] and that increasing-velocity trajectories can be caused by an unstable integrator.[30] A tonic imbalance in the vertical semicircular canal-ocular pathways has been postulated.[22,23,54] Baloh and Spooner[22] suggested that both upward pursuit and downward pursuit are impaired. The apparent superiority of upward pursuit might be due to an upward slow-component velocity of the nystagmus that varies with changes in vertical gaze position. An imbalance in the otolith-ocular reflex has also been suggested to be the cause of DBN.[53]

The findings in this study do not allow us to choose among these mechanisms. However, our observations demonstrated that the waveform of the slow component is variable and should be used with caution to verify a model of DBN. The presence of constant-velocity, increasing-velocity, and decreasing-velocity trajectories can be interpreted as showing that different mechanisms exist among our group of patients. However, waveforms changed in different positions of gaze in some patients in our study, and waveforms can vary from beat to beat in the same patient.[45] The effects of positioning are consistent with abnormalities within the vertical vestibular or otolith systems, but do not prove that they exist. It is likely that detailed knowledge of the pathophysiology of DBN must await additional studies in experimental animals, in which the anatomy and physiology of vertical ocular motor pathways within the cerebellum are revealed.

SUMMARY

Clinical examinations and eye movement recordings of 91 consecutive patients with DBN were analyzed to describe the characteristics of DBN and to localize the lesions producing this abnormality. Horizontal and vertical eye movement recordings were made with EOG and/or magnetic search coil. The most frequent causes were infarction, cerebellar and spinocerebellar degeneration syndromes, MS, and developmental anomalies affecting the pons and cerebellum. Toxicity from anticonvulsant drugs probably caused nystagmus in a few patients. Clinical examinations, excluding electronic eye movement recordings, were used to localize lesions. Localizations included the cerebellum in 88% of the patients. However, localizations to structures outside of the cerebellum were made in several patients.

The effects of DBN of gaze position, convergence, blockage of fixation, and positioning of the head and body were observed. Almost all patients had DBN in some position of gaze while sitting and fixating a distant target. A few patients demonstrated DBN only with convergence, in the dark, or with positioning of the head and body. Horizontal gaze increased DBN in most patients. The nystagmus slow components usually had constant-velocity or increasing-velocity waveforms. The effects of vertical gaze on DBN were variable. In general, statistically significant differences in the frequencies of these effects among the various causes and localizations of lesions were not found.

Horizontal eye movements were electronically recorded in DBN patients, in a group of normal subjects, and in a group of patients with isolated cerebellar atrophy who did not have DBN. The pattern of abnormal horizontal eye movements characteristic of damage to the midline structures of the cerebellum (impaired pursuit, impaired OKN, and inability to suppress VOR) was found in almost all DBN patients (99%), including patients with lesions localized to structures outside the cerebellum by clinical examination. DBN is usually produced by lesions in the cerebellum that also damage pathways that control horizontal tracking and visual-vestibulo-ocular interactions.

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